

American Journal of Obstetrics and Gynecology

VOL. 29

MARCH, 1935

No. 3

Original Communications

INTESTINAL COMPLICATIONS RESULTING FROM PRO- LONGED RADIUM AND X-RAY IRRADIATION FOR MALIGNANT CONDITIONS OF THE PELVIC ORGANS*

THOMAS E. JONES, M.D., CLEVELAND, OHIO
(*From the Cleveland Clinic*)

LAST year, before this Society,¹ Dr. Palmer Findley presented a paper on the complications of radium therapy for carcinoma of the cervix, and it is not my intention at this time to repeat those varied adventitious circumstances which he covered so well, but merely to call your attention to the possibility of intestinal injury by radiation therapy and the importance of its recognition.

The present study directs attention to a rather new clinical entity² which may develop and call for surgical intervention many months or years after complete regression or cure of the cervical cancer. In a series of 520 patients with cervical carcinomas, who received irradiation therapy at the Cleveland Clinic, there have been seven known cases of benign stricture of the intestine causing obstruction which might easily have been construed as, or confused with, metastatic deposits. In five of these cases the obstruction was in a movable segment of the sigmoid and in two cases in the small intestine. All these strictures were observed in patients who had been irradiated for carcinoma of the cervix, but the increasing use of radiation for other conditions which necessitate exposure of the intestines may result in similar complications. Subsequent to the irradiation therapy no evidence of

*Read at the Forty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., September 6, 7, and 8, 1934.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

carcinoma was found in these cases, and judging by present-day standards, none of these patients received excessive irradiation. Since similar methods of therapy are in general use, it seems probable that the incidence of the lesion is greater than is surmised at the present time; and if similar cases have been attributed to metastasis in the past, the mortality statistics relating to metastasis from cervical carcinoma are open to question. Desjardins³ in an exhaustive report has called attention to intestinal injury produced experimentally by irradiation.

There are many reports dealing with the manifestations of acute injury of the intestine following irradiation, both experimental and clinical, but I have not been able to trace any reports on patients who have recovered from the acute symptoms and have later developed the chronic condition herein described. If such cases have been described this report adds seven cases of intestinal obstruction which developed in patients eight months to eight years after radiation therapy for cervical carcinoma.

The rate of recurrence of cancer is so high that almost any abdominal or pelvic pain may quite naturally and logically be attributed to malignant extension or metastasis. If the condition actually is a benign stricture caused by irradiation, it is quite obvious that additional x-ray treatment would only aggravate the condition and hasten the end. Therefore, one should always keep in mind the possibility that a patient who exhibits unusual abdominal symptoms, particularly if they simulate intestinal obstruction, several months or even years following radiation therapy, may have a stricture of the intestine and may be restored to normal health by resection of the lesion. Before attributing this disability to metastasis, thorough re-examination by sigmoidoscopic and roentgenographic studies should be made to eliminate the possibility of this curable complication. While roentgen ray examinations demonstrate lesions in the sigmoid quite readily, strictures in the small intestine are quite difficult to visualize unless the obstruction is practically complete. In this type of case it is inadvisable to give barium in any large amounts, and therefore exploratory operation is warranted; especially in patients in whom there is no evidence of recurring carcinoma in the pelvis.

CASE REPORTS

CASE 1.—A woman, aged sixty years, when first examined had a carcinoma of the cervix uteri, extending into the broad ligament. Biopsy made at the time of treatment showed a squamous cell carcinoma, and the patient was treated by irradiation with radium and roentgen rays.*

*One tube containing 170 mc. radon was inserted into the cavity of the uterus and cervical canal for twelve hours, producing a total irradiation of 2,040 mc. hours. Three days later, roentgen therapy was started. Two months later a second radium treatment was administered to the cervix, using 220 mc. of radon in four tubes against the cervix for ten hours, totaling 2,200 mc. hours, or a total of approximately 4,240 mc. hours for the two radium treatments. The actual amount of radiation received represents about 3 per cent less than these figures when calculated according to the time the radon is in place.

Follow-up examinations had shown no evidence of malignant disease, and the patient had been in excellent health for over two years after the last radium treatment. Then she began to have unusual constipation, which became progressively more severe and at the time of readmission, a few weeks after its onset, she had symptoms and signs of intestinal obstruction. Proctoscopic examination yielded no information and neither blood nor mucus was seen in the bowel. Roentgen examination of the colon revealed an obstructing lesion in the sigmoid colon, which was believed to be due to carcinoma. At operation, the lesion had the characteristics of a benign stricture. There were bands of adhesions encircling the sigmoid colon at the site of the lesion, and these were attached to the fundus of the uterus. The adhesions were severed, this portion of the colon was resected, and an end-to-end anastomosis was made. The pathologic diagnosis was chronic inflammation. The patient made a good recovery from the operation, and has reported normal health on numerous occasions during the two and one-half years since the resection was performed.

CASE 2.—The patient, aged fifty-two years, had had a pelvic abscess years previously, and came to the Clinic because of pelvic pain. The cervix uteri was firm, enlarged, and nodular, especially on the right side, and bled easily. There was no thickening of the broad ligaments. Squamous cell carcinoma was revealed by biopsy and radium and roentgen therapy was administered.*

For a year and a half after the irradiation, follow-up examinations had shown no evidence of disease, and the patient had been in excellent health. Then she began to have severe pains in the bladder, associated with some blood in the urine. These symptoms persisted for three weeks. When the patient returned to the Clinic, cystoscopic examination revealed several submucous hemorrhages on the posterior wall of the bladder, in the center of which was a white, irregular area about 2.5 cm. in diameter. Subsequent examinations showed a definite ulcer in the irregular area mentioned. One year following the initial cystoscopic examination, the ulcer had disappeared completely, except for a small area of submucous hemorrhage due to separation of the slough a few days previously.

Approximately a year and nine months subsequent to treatment the patient began to have unusual abdominal symptoms, simulating intestinal obstruction. Roentgen examination of the colon showed no obstruction at the time of the onset of these symptoms. No further roentgen studies were made. The initial attack soon subsided, but two months later there was a recurrent attack which was more severe, and operation was performed. There was an old inflammatory process in the uterine tubes, but no evidence of carcinoma could be found. About 25 cm. proximal to the rectum there was a definite, almost complete obstruction of the sigmoid colon. It was not adherent to the pelvis. It seemed as if there were a cicatricial band in the bowel wall, with very little inflammatory reaction outside. Resection was considered, but it was deemed more advisable to make an anastomosis around the obstruction, particularly in view of the fact that the sigmoid colon was unusually long. A side-to-side anastomosis was made. The last follow-up letter from the patient, five years after operation, states that she is in normal health.

CASE 3.—The patient, aged forty-one years, had an enlarged cervix uteri which was bleeding and ulcerated. The principal involvement was inside the cervix, extending into the uterus and outward through the cervix, lateral to the external os. The biopsy showed squamous cell carcinoma. Radium and roentgen therapy was administered.†

*Two tubes containing 305 mc. of radon were inserted into the uterus and cervix and two tubes containing 140 mc. of radon were placed against the cervix for six and a half hours producing a total irradiation of about 2,759 mc. hours. Twelve days later roentgen therapy was started.

†One tube containing 106 mc. of radon was placed in the fundus of the uterus, one tube containing 247 mc. of radon was placed in the cervix, and four tubes containing 142 mc. were placed against the cervix for eight hours, or a total of approximately 3,960 mc. hours. One month later roentgen therapy was administered.

The frequent transitory rectal sequelae immediately following these treatments were prolonged in this case. For six months, the patient complained of loose stools containing unusual quantities of mucus. It is significant to note here that there was no lesion in the rectum opposite the treated area where one would presume the maximum effect of radium would prevail. The following months there was marked constipation, and after a period of eleven days without a stool, the patient suffered from considerable abdominal distention, and was readmitted to the hospital with a diagnosis of intestinal obstruction. Follow-up examinations had shown no evidence of recurrence of the malignant growth in the cervix or adnexa. Proctoscopic examinations had shown no evidence of disease. Laparotomy was not performed at this time, since her symptoms were relieved by the use of enemas and hot fomentations over the abdomen.

She was readmitted to the hospital at two- and six-month intervals subsequently. An attempted barium enema was expelled as soon as it had reached the sigmoid colon, apparently indicating obstruction at this level.

Fifteen months after irradiation a cecostomy was done and a large tube was inserted for irrigations. Later, a colon roentgen examination, during which the barium suspension was injected through the colostomy tube, revealed a definite obstructing lesion in the sigmoid colon. At the subsequent operation, performed recently, the lesion proved to be a benign stricture causing complete obstruction. This portion of the colon was resected, and an end-to-end anastomosis was made. The patient's recovery following operation was uneventful and the cecostomy closed itself.

CASE 4.—The patient, fifty years of age, had a diffuse carcinoma of the cervix uteri, involving chiefly the cervical canal (Stage 1). Squamous cell carcinoma was revealed by biopsy and the patient was treated by irradiation.*

Subsequent examinations revealed satisfactory progress, and the patient was in good health except for an attack of gallstone colic. Approximately three years following irradiation, she stated (for the first time) that she had had some blood in the stools off and on during the previous year, which she attributed to hemorrhoids. Unusual constipation was also present. Pelvic and proctoscopic examinations showed nothing except the hemorrhoids, and those were treated by the injection method. A colon roentgen examination, however, revealed an annular filling defect in the sigmoid colon, and reexamination one month later revealed the same finding. Bleeding continued at intervals and in one instance a cupful of blood clots was passed.

At operation (three and one-half years following irradiation) the lesion proved to be a benign stricture. This portion of the colon was resected and an end-to-end anastomosis was made. Death from local peritonitis followed, fifteen days after the operation.

CASE 5.—The patient, aged fifty-nine years, suffered from a rather extensive carcinoma of the cervix uteri, involving chiefly the anterior lip of the cervix and extending into the vaginal wall. The lesion, as determined by biopsy was a squamous cell carcinoma. The patient was treated by radium irradiation,† but received no roentgen therapy.

*Two tubes containing 244 mc. of radon were inserted, one in the cervix and one against the cervix, for ten hours, or a total of approximately 2,440 mc. hours. One month later, roentgen therapy was administered.

†The tube containing 266 mc. of radon was inserted into the cervical canal and ten radium needles, each containing 10 mg. of radium were inserted into the carcinomatous mass, approximately 1 centimeter apart; and one tube containing 107 mc. of radon was placed against the anterior lip of the cervix, a total of 373 mc., of radon and 100 mg. of radium for 7½ hours, equivalent to about 3,729 mc. hours.

The patient made satisfactory progress but complained of slight constipation which was unusual for her. Seven months following radium irradiation she stated that during the past few weeks the constipation had become more severe and that she had passed darkened blood, blood clots, and mucus by rectum, associated with cramplike abdominal pains. Pelvic examination showed nothing of significance, but roentgen examination of the colon revealed a conical, fixed, concentric narrowing in the midsigmoid area, believed to be due to an irradiation stricture. At operation the stricture was immediately behind the fundus of the uterus. This area appeared to be anemic as compared with the remainder of the sigmoid colon. A cecostomy was performed and one month later a resection of the lesion, and an end-to-end anastomosis. The patient was discharged from the hospital one month after operation, at which time the stools were normal.

CASE 6.—The patient, aged fifty-eight years, had a carcinoma of the cervix uteri, involving chiefly the posterior lip and the posterior vaginal wall. The pathologic diagnosis was squamous cell carcinoma. Radium therapy was followed by roentgen irradiation.*

For five months the patient showed satisfactory progress with complete regression of the lesion, but did not return for the usual subsequent examinations. Two months later, in a letter from the patient's husband who was a physician in a distant town, it was learned that the patient had been confined to bed for a month because of abdominal pain, nausea, and pronounced vomiting. He stated that examination revealed no evidence of carcinoma in the cervix or in the neighboring structures. Death followed one month later. Autopsy was performed which revealed an inflammatory stricture of the small intestine, causing a definite obstruction. The exact relation of this area to the uterus was not stated, but examination of this area of the intestine and the uterus, after removal from the abdomen, revealed adhesions on the peritoneal surfaces of both.

From these findings it may be inferred that the stricture of the small intestine involved an area adjoining the uterus, that fibrous adhesions formed between the two, and that the cause of death (since no other cause was considered or found) was severe toxemia, resulting from obstruction of the small intestine.

CASE 7.—The patient, aged forty-two years, was admitted to the Clinic on the first of June, 1926, with a history of vaginal bleeding for one year. Examination showed extensive papillary carcinoma of the cervix with involvement of the vaginal wall anteriorly and posteriorly, but apparently there was no invasion of the broad ligament. Radium and roentgen irradiation were administered in June, 1926.†

About six months later the patient reported that for a month she had been having trouble with her rectum. The symptoms included tenesmus, mucus, and blood in the stools; this gradually subsided and when the patient was examined a year after treatment there was a narrowing of the rectum opposite the cervix, but the opening easily admitted the index finger. The patient had no abdominal complaints.

In October, 1930, more than four years after irradiation, the patient complained of recurring attacks of abdominal pain which her doctor attributed to gallbladder disease. Roentgenographic examination of the gastrointestinal tract at that time showed no abnormality except a nonfunctioning gallbladder. The attacks of pain continued at occasional intervals until March, 1934, when she suffered a very severe

*One tube containing 118 mc. of radon was placed in the cervix and another tube containing 177 mc. of radon was placed against the posterior lip of the cervix, for ten hours, or a total of approximately 2,950 mc. hours. One and a half months later roentgen therapy was administered.

†The first application of radium consisted of 3,384 mc. hours with tubes and needles in and against the cervix, and roentgen irradiation was given about three weeks later. A second application of radium to the cervix, amounting to 1,300 mc. hours was administered about a month after the roentgen therapy.

attack, was ill with abdominal pain, nausea, and vomiting for two weeks and lost a great deal of weight. She reentered the Clinic Hospital on April 7, 1934, nearly eight years after the course of radiation therapy. While at the time of hospitalization, there was no evidence of obstruction it was felt that the last attack simulated an obstruction and operation was advised.

Exploratory laparotomy was performed on April 10, 1934. In the small intestine, 3 feet from the ileocecal valve there was an almost complete obstruction with collapse below and considerable dilatation above the stricture. About 4 inches above this there was a slight narrowing of the lumen. A resection of about eight inches of small intestine and an end-to-end anastomosis was made. The patient made an uneventful recovery and was out of the hospital on the fourteenth day. On the fifteenth postoperative day she experienced a sudden severe pain in the right lower quadrant and some abdominal distention, but there was no elevation in temperature or increased pulse rate. The patient was treated expectantly for five days apparently satisfactorily, when distention recurred and exploration was done. There was some free fluid in the abdomen and some distended coils of intestine one of which was used for ileostomy. This functioned quite satisfactorily but the patient gradually failed and died, about two weeks later, on May 13, 1934.

Pathologic Report.—Microscopic: A longitudinal section of the small intestine showed marked thickening and dense fibrosis of the serosal coat, in which there were large numbers of greatly thickened arteries, showing varying degrees of obliterative endarteritis, degeneration of the lamina elastica, and hyalinization of the intima, with no calcification present. In some areas, there was localized, perivascular, inflammatory infiltration, with plasma cells predominating. There was considerable, diffuse increase of fibrous tissue in the muscular coat, and fibrosis of the submucosa. The mucosa was somewhat atrophic, contained very little lymphoid tissue and showed mild, diffuse, inflammatory infiltration, with numerous eosinophiles and plasma cells present. In one area, there was active ulceration, with almost complete destruction of mucosa. The base of the ulcer extended into the muscular coat. There was some fibrinous exudate and many leucocytes, together with plasma cells, eosinophiles, and lymphocytes in the exudate. Ganglion cells of the submucosa showed extensive degenerative changes in the neighborhood of the ulcer. There was no evidence of neoplasm.

DISCUSSION

This group of cases is of particular interest to me because I administered the radium in all cases and have had the surgical management of the resulting complications. The x-ray therapy was administered by Dr. Portmann. Obviously, as is the case in any pathologic process the factor of particular interest is the causation and possible prevention of the lesion. In this case the radium therapist is likely to blame the x-ray therapist and vice versa, whereas both probably have contributed to the causation of the lesion. It is significant to note that in this series only one patient had any lesion in the rectum opposite the cervix where the maximum intensity of radiation would be delivered. In Case 7 with the obstruction of the small intestine there was a slight narrowing of the rectum which was readily dilatable. This would seem to justify the statement that the radium dosage used in this series was not excessive.

That roentgen irradiation is not entirely responsible is a justifiable assumption, since one patient (Case 5) received no x-ray therapy. Furthermore the lesion in this case was not at the point of maximum intensity but in the sigmoid several inches away. One then must search for causes which contribute to fixation of a certain loop of small or large intestine in the pelvis which is the recipient of the maximum radium and roentgen dosage at that particular point. Previous inflammatory disease of the pelvic organs, either specific or post-partum, might tend to fix a loop at a vulnerable point, yet this was not a factor in this group of cases because in only one was the bowel fixed in the bottom of the pelvis by an apparent previous inflammatory process.

From my observations I would venture the following explanation which may apply in the majority of cases: The initial insult is delivered by radium. If a loop of small or large intestine remains in the same position in the culdesac during the entire time of radium irradiation, the erythema produced at this point may be sufficient to produce a simple local peritonitis which would fix the bowel at this point temporarily. Before the exudate is completely absorbed, roentgen rays are administered, thus furnishing additional irritation which is sufficient to cause an ulceration in the mucosa, and eventually goes on to stricture formation. As time passes the exudate is absorbed and the bowel becomes free, which is the general finding at operation.

Whether this intestinal lesion be due to one agent or the other or a combination of both, it behooves us to devise ways and means to prevent it. Change of position of the patient during treatment suggests itself as an aid, but this would not be entirely safe because of the danger of dislodging the radium tubes and possibly causing damage to the rectum or bladder. However, a Trendelenberg position maintained during treatment may help to keep the intestines out of the pelvis while the latter is being irradiated both by radium and x-rays. If the theory of some fixation of a loop of intestine is tenable, drugs to stimulate peristalsis may be considered, and it might be advisable to give $\frac{1}{2}$ to 1 c.c. of pitressin every four hours while the radium is in place or just previous to an x-ray treatment, in order to keep the intestines moving, and thus, to preclude excessive irradiation of any one loop.

In presenting these intestinal complications I do not wish to convey the idea that I disparage the present-day treatment of cancer of the cervix. I believe it is the best we have to offer and I shall continue to use it. However, on the basis of the experience here reported, I would interject a word of caution regarding the step that is being taken at the present time, the stepping up of the voltage many times more than has been customary, because I think increased voltages carry a definite potential danger of damage to the intestines.

CONCLUSIONS

The recognition of the possibility of benign stricture of the intestine as a complication following radiation therapy often months or years later, is of utmost importance, for it can very easily be confused with recurrence of malignancy. Its detection and surgical treatment may salvage the lives of many patients otherwise regarded as having hopeless malignancy.

REFERENCES

- (1) *Jones, T. E.*: J. A. M. A. **99**: 380, 1932. (2) *Collins, E. N., and Jones, T. E.*: Surg. Gynec. Obst. **59**: 644, 1934. (3) *Desjardins, A. U.*: Am. J. Roentgenol. **26**: 145, 336, 493, 1931.

2026 EAST NINETY-THIRD STREET

A CRITICAL STUDY OF FIVE HUNDRED CASES OF ECLAMPTOGENIC TOXEMIA*

FREDERICK H. FALLS, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, University of Illinois,
College of Medicine)

THESE data have been compiled from an analysis of five hundred consecutive cases of eclamptogenic toxemia occurring in my clinics at the University of Illinois and the University of Iowa in the last twelve years approximately.

The reason for this presentation is to bring before you the results of a simple management, adaptable to any clinic or hospital or the private practice of any well-trained physician. It is also hoped that it may throw some light on some of the moot questions in eclampsia, such as the danger of operative interference, whether or not cesarean section is justifiable, whether or not the phenolsulphonephthalein test is of prognostic value.

The series is relatively small, but it has the advantage of having been slowly accumulated under one system of treatment which has not been deviated from appreciably from year to year. The management of practically the entire series of patients has been under my personal supervision. Almost all of the cesarean sections have been done by me. Forceps deliveries, versions, and bag inductions of labor have been done by me or my residents.

That part of the clinical material gathered in the University of Iowa was composed for the most part of young, illegitimately pregnant

*Read at the Forty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., September 6, 7, and 8, 1934.

girls who were sent in from the surrounding country about the twenty-eighth week to stay in our prenatal home until confinement. They were under the close supervision of a nurse housekeeper who followed instructions as to their diet and exercise. They were seen twice a week routinely by students and interne; the blood pressure readings were taken and the urine specimens were examined. All patients showing even moderate grades of toxemia were sent into the hospital.

The Illinois group were all charity cases from the slums of Chicago. Most of them were ignorant women, many difficult to instruct because of their limited knowledge of English. They were seen routinely in our prenatal clinic by my associates who sent into the hospital all patients showing evidences of toxemia which did not yield readily to home management in a few days.

All cases were ward patients, none had private nursing care or any special attention beyond what would be ordinarily given a sick patient in an obstetric ward. It is obvious, therefore, that no specially favorable factors entered into the care of these patients to account for our results. Those patients who delivered spontaneously or by breech extraction were delivered by the internes or resident physician, in most cases without the presence of a member of the teaching staff.

As I have stated before, our conception of eclamptogenic toxemia is a metabolic disturbance due to overproduction of protein split products, or to decreased detoxification of the same, or both. These toxins circulating in the blood act first and most powerfully on the highly specialized cells of the body, especially those which have to do with their detoxification and excretion, the liver and kidney. Damage to these organs completes the vicious circle and the level of the toxins in the blood rises unless the production of the toxins is curtailed or the reserve power of the kidney and liver are sufficient to overcome the difficulty by elimination of the toxins or by neutralizing them.

This view has much in it comparable to that expressed by Solomons before this body two years ago, although he feels that reduction in proteolytic ferment content of the blood may be an important factor. Our work on the Abderhalden test in 1914 seemed to show the ferment content of the blood increased in eclamptogenic toxemia.

The brain, the heart muscle, and the retina are also secondarily affected by the intoxication which results in decrease in their functional efficiency.

We believe nephritic toxemia to be an eclamptogenic toxemia fostered by the inability of the kidney to eliminate at the usual rate the normal amount of toxins produced by a normal pregnant woman.

We feel that it is a mistake to confuse the issue by splitting up the cases of eclamptogenic toxemia into low reserve kidney (Stander),

eclampsism, preeclampsia, and eclampsia. It would be equally logical to divide lobar pneumonia into one lobe pneumonia or two lobe pneumonia, or to speak of one kind of typhoid fever with perforation or hemorrhage and another kind without. If a patient has chronic nephritis and develops diabetes, it may alter the course and symptoms of the diabetes, but the fundamental cause and effect of the diabetes remain the same.

Hofbauer has a very similar conception of the etiologic factors concerned in the disease. He stresses the importance of the posterior pituitary hormone as a contributing factor, producing angiospasm which results in tissue anoxemia, especially in liver, kidney, heart muscle, and brain.

The sources of the toxins are three in number: (1) The fetus and placenta, (2) the exogenous protein metabolic products, and (3) the products of endogenous protein metabolism.

The control of these sources of intoxication is only partially possible. In our opinion little if anything can be done to regulate the toxins produced by the fetus and placenta. Our conception of these structures is that biologically they are comparable to a malignant tumor and can be about as easily influenced by ordinary measures.

The exogenous protein metabolism can be controlled by the nature and amount of food intake. The endogenous protein metabolism can be reduced significantly by restricting bodily activity, thus reducing the protein split products from this source.

The level of toxins in the blood from all of these sources can be minimized by stimulating bowel activity with magnesium sulphate, by promoting diuresis, and by venesection.

PROCEDURE

The patients as they enter our clinic are immediately put at bed rest and given nothing but milk by mouth. They may have a quart or more a day. An ounce of magnesium sulphate is given night and morning until watery stools are obtained, after which it is given only in the morning. A phenolsulphonephthalein test is run according to the original Gerrhety and Roundtree technic of intramuscular injection. I find that nearly every interne has his own ideas as to how the test should be performed, and only by insisting can one expect to have it done properly and thus have the results comparable with other cases.

A catheterized specimen of urine is examined. A blood pressure reading is taken and recorded night and morning, in all cases where it is above 140 mm. When the pressure drops and the albumin disappears, fruits and vegetables are added to the diet, and the patient is permitted room exercises. If the symptoms do not reappear and the patient is not at term, she is sent back to the out-patient service for bi-weekly prenatal observation.

If she does not respond thus favorably, labor is induced by quinine and castor oil, or if this fails, bag induction is used. In some cases, especially in elderly primiparas, it has been our practice to resort to cesarean section under these circumstances because of the uncertainty of our induction methods, and since we favor taking a slight additional maternal risk for the sake of the baby in these patients.

With a rapidly advancing toxemia there may not be time to try out the conservative management. In these cases we start the eliminative treatment as usual, and at the same time start the induction of labor. Bag induction is used in most cases. If there is a significant pelvic contraction, an organic heart lesion, or other conditions which might become a serious complicating factor in attempting to deliver from below, we do a cesarean section.

In the fulminating cases which go on to convulsions within a few hours after the premonitory symptoms, we do a cesarean section immediately.

Patients admitted in labor showing severe symptoms or in convulsions are treated palliatively with morphine and chloral hydrate per rectum until complete dilatation of the cervix results. If the second stage lasts more than half an hour, labor is terminated by forceps or version, depending upon whether the head is or is not engaged.

Postdelivery, all except the patients with very mild eclamptogenic toxemias are treated as if we expected them to develop convulsions. They are kept on a milk diet until the albuminuria decreases, and the blood pressure declines. It is difficult to convince the internes and resident physicians that all danger is not past as soon as the baby is born. Continued management, however, prevents postpartum convulsions in most cases, or if they occur, it lessens their severity.

CLINICAL OBSERVATIONS

The patients were found to be young for the most part. Twenty per cent were less than twenty years of age, about 50 per cent were between twenty and thirty, and 28 per cent between thirty and forty. This agrees well with the fact that 54 per cent occurred in primiparas, 12 per cent in para ii, 11 per cent in para iii, 3 per cent in para iv, and 12 per cent in para v or over.

These figures compare with those of practically all writers on eclampsia and require an explanation. No very satisfactory explanation of this point appears in the literature. It is difficult to see why women when young and vigorous before they have had a chance to develop serious degenerative lesions in the kidney, liver, heart, and brain should be less resistant to any toxic state than older women. Paramore believes that increase in intraabdominal pressure in these women is the important feature. Alvarez thinks that increased intraabdominal pressure leads to increased permeability of the bowel wall to incompletely broken-down end-products of digestion caused by vascular stasis in the bowel.

The explanation lies, we believe, in the fact that the pregnant state fundamentally requires a marked change in the activities of the glands of internal secretion. The changes are reflected in marked alterations in metabolism. For the primipara undergoing this experience for the first time, the fluctuations may be more marked and the compensatory mechanism less well adjusted than in the woman who has undergone the experience several times. As a result an apparent immunity is developed in the multipara which, however, should not be confused with immunologic reaction in the ordinary sense.

Headache, severe enough to be noted as an important complaint, was noted in 272 of these women.

Pitting edema was found in 325 patients and all cases were excluded from consideration which seem to be on other than a toxic basis. We could not confirm the observation of Williams that lack of edema in eclamptic patients seems to be associated with the more toxic cases.

Visual disturbances were noted in 126 patients. They varied from a slight blurring to inability to count fingers at a few feet distance. None of the patients

showed complete blindness even for a short time. This frequent functional impairment was in marked contrast to the paucity of cases showing changes in the eyegrounds.

Epigastric pain was complained of in 156 cases and was associated with vomiting in 205 cases. These symptoms we feel are due to the irritation of the abdominal and pelvic sympathetic ganglia by the toxins.

Twenty-nine of the five hundred patients developed convulsions in spite of our management. Of these only 13 developed convulsions antepartum. We feel that our conservative management in most cases, and our prompt intervention in those cases not yielding to conservative management, resulted in reducing the number of patients having convulsions, as well as the number and severity of convulsions in each case.

Sedatives were not given to control convulsions in any patient until after the uterus was emptied, even the usual preoperative $\frac{1}{4}$ gr. of morphine sulphate was omitted in patients requiring cesarean section. On the other hand, morphine and other sedatives were used freely following delivery in all patients in whom convulsions had occurred and in many patients in whom it seemed probable that convulsions were imminent.

Magnesium sulphate injections were used in doses of 20 c.c. of a 10 per cent solution in a few of the milder cases where the patients had convulsions.

Since magnesium sulphate was withheld purposely in all but a few of the cases, it is evident that it is not essential to the management. Treatment by glucose injections as recommended by Titus was withheld for the same reason.

Albuminuria occurred in 265 cases in amounts more than a trace. Red blood cells appeared in 132 cases, hyaline casts were found in 122 cases, and granular casts were present 137 times. These findings stress the fact that the kidney is very little damaged in nearly half of the cases. Some of the 265 patients may have presented albuminuria before they become pregnant.

A phenolsulphonephthalein test was done on 153 patients. The original Gerrhety and Roundtree technic was followed: injecting exactly 1 c.c. of the dye intramuscularly and waiting until the dye appeared in the urine before starting the collection of the first one-hour sample which was voided. The bladder was catheterized at the end of the second hour and the percentages estimated by the Dunning colorimeter. In no cases where convulsions occurred was there a normal or near normal reading. The patients who had the lowest percentage dye excretion were clinically the most seriously affected. Mild eclamptogenic toxemias had in some instances normal or above normal readings. A low excretion, less than 15 per cent in two hours is a serious prognostic sign.

Early in the series the eyegrounds were studied in 23 cases. All of the observations were made by ophthalmologists. Of these patients, one presented a mild arteriosclerosis, two a slight edema and sclerosis, and the rest showed no lesion characteristic of serious intoxication. Most of the negative eyegrounds occurred in patients with serious intoxication in whom it was hoped the findings might help to differentiate between the nephritic and preeclamptic toxemia or might furnish an indication for radical intervention. The results were so disappointing that further study was discontinued.

INTERFERENCE

Induction of labor was undertaken in two groups of cases: Patients under treatment who failed to respond to medical management, and those who entered the clinic in such serious condition and with a history of such a sudden onset of symptoms that conservative measures seemed contraindicated. Labor was induced by quinine and castor oil in 78 patients. Bag induction was used in 72 cases. The membranes

were ruptured artificially in 110 cases. In some patients all three of these procedures had to be applied to bring about labor. In general, it was noted that bag inductions or rupture of the membranes was necessary in all except those patients who were at or near term or in whom it was evident that an unusual irritability of the uterus made premature labor probable. For this reason in primiparas and especially in elderly primiparas who were not within two weeks of term, cesarean section was frequently the method chosen for delivery to avoid the uncertainties of induction, especially in rapidly advancing toxemias. Rupture of membranes was especially indicated in multiparous patients at term or in the early stages of labor. This procedure was never used when cesarean section was considered as even a remote possibility as the method of delivery. There was no more morbidity than would be expected from an equal number of nontoxic patients delivered in the same way. This speaks against the view of Williams, DeLee, and others that the eclamptogenic woman is especially liable to infection.

Of these 500 patients, 396 were delivered spontaneously which, I believe speaks for itself, as to the conservative attitude toward these cases in our clinic. Forceps were used in 38 cases all of which were midforceps or low forceps. Version and extraction were done 18 times. The indications for these operations were mixed. Only a small percentage were done for the sole indication of toxemia of pregnancy. In most cases an important contributing indication was present, such as a long second stage, rigid perineal muscles, contracted pelvis, cardiac lesions or evidence of maternal or fetal exhaustion.

Cesarean section was done in 25 cases. In practically all of these the most serious types of toxemia that were seen in the entire series were present. We use this method of delivery especially in the patient with a sudden attack of toxemia who is clinically normal in the morning and who may be dead by night with all the signs and symptoms and postmortem findings of eclampsia.

Our conception of the pathogenesis in these cases is that the fetus and placenta are nearly always responsible. A sudden release of toxin overwhelms the defense mechanism. This may be due to infarcts in the placenta as Young thinks. Many patients showing placentas with very extensive infarct formation show absolutely no signs of eclamptogenic toxemia. There may, however, be differences in the kind of infarct or in the speed with which they develop to account for the appearance of toxic symptoms.

In these patients with a fulminating toxemia we do a cesarean section as soon as the necessary preparations can be made. Striking directly in this way at the source of the toxins would seem to be the logical method of approach when proper facilities are available.

An important factor in this connection is a prompt decision as to what should be done and rapid execution of the plan. Delay and temporary conservatism to see whether the convulsions become more frequent or stronger and whether or not they may be controlled by medical management, while successful in many cases will not give as good results in the long run.

The other group of patients who were delivered by cesarean section were the more slowly advancing toxemias who in spite of adequate medical management continue to grow worse and in whom induction of labor from below seems to be contraindicated.

Cesarean section is never the operation of choice in the delivery of a patient with eclamptogenic toxemia, but it may very well be the lesser of two evils when the dangers to both mother and child from further continuance of the pregnancy or a delivery from below are considered.

Local anesthesia or a combination of local and ethylene anesthesia was used in all cesarean operations.

One of the patients who had a cesarean section died of a general peritonitis following a classical operation. She had no convulsions. The operative mortality, therefore, would be 4 per cent in this series of cesarean operations.

The babies of eclamptogenic toxemia patients were found to be, as a rule, less well developed and less vigorous than babies from normal women. The toxic state of the mother reflects itself on the child if present for a long time before the birth of the baby or if it is of very severe grade. Therefore the greatest attention should be paid to the proper conduct of the labor to prevent undue pressure on the babies head and to protect it from shock and exposure as soon as it is born. Frequently the attention of the doctor and nursing personnel is so focused on the condition of the mother that as a result the welfare of the baby may be neglected immediately after birth, much to its detriment. We prepare in each case for the reception of an undernourished, asphyxiated baby that is toxic and in some shock. If there is considerable prematurity, we dilate the perineum manually and do a lateral episiotomy to prevent undue pressure. The use of local anesthesia to block the perineal nerves is of value, since it serves to relax the perineal muscles and decrease pressure on the fetal head. Furthermore it reduces painful stimuli from the stretching perineum, and cuts down very materially the amount of inhalation anesthesia necessary for obstetric analgesia or replaces it entirely.

Careful attention to the premature infant who should be placed in an incubator for at least twenty-four hours is very important. Oxygen is used for blue spells, and the trachea is kept clear of mucus by gentle suction with the tracheal catheter when necessary. Food is a secondary consideration until respiration is satisfactorily established, after which we give small amounts of mothers' milk diluted to half strength and fed by a medicine dropper or gavage as the strength and aptitude for feeding of the infant seems to indicate.

Failure to recognize the precarious condition of these toxic premature babies has, we feel, resulted in the unnecessary loss of a considerable number of lives.

There were 66 fetal deaths in the series. Of these, 38 were babies from mothers with a diagnosis of eclamptic and preeclamptic toxemia and 28 were babies from mothers with a nephritic toxemia. Twenty-five of the 66 babies were born alive and died before leaving the hospital. All babies that went home with their mothers were in good condition on leaving the hospital.

The cause of death was the toxemia in eight cases as nearly as could be determined. The cause of death in one other case was cord hemorrhage and syphilis. Of the babies born dead 25 were stillborn without maceration, 23 were macerated, 15 were under 2,000 gm., 2 were marked deformities or monstrosities. There was a gross fetal mortality of 11.2 per cent. The corrected fetal mortality in babies over 2,000 gm. who died from no other obvious cause than toxemia was 1.6 per cent. Twelve babies who were born alive and died were from mothers classified as eclamptic or preeclamptic, giving a mortality for this group of 2.2 per cent; of the 12 only 4 were viable babies. The cause of death in all was atelectasis and pneumonia as shown by postmortem examination. Only 4 of the 12 babies were over 2,000 gm.

Of the babies from nephritic toxemic mothers, 13 were born alive and died, a mortality of approximately 40 per cent. Only 4 of the 13 babies were over 2,000 gm.

The Wassermann test was found to be positive in only 4.6 per cent of 418 cases. This is relatively low, for in normal pregnant women we found it to be 13.6 per cent in a similar group of cases (Falls and Moore).

Of the 500 cases of eclamptogenic toxemia, 403 were preeclamptic according to the Williams classification, 29 were eclamptic and 68 were nephritic. We recognize the pitfalls in attempting to classify cases in this manner from clinical evidence, but the classification was made only after careful prenatal history and postnatal observa-

tion. It was found impossible with the facilities at our command to follow up each case over a period of months and years to help determine the classification to which it should belong.

Two of the women in this series died. Neither of these patients had gone on to the convulsive stage. Viewing the cases in retrospect, it would seem that those deaths occurred from failure to adhere rigidly to the scheme of treatment herein outlined.

FATALITIES

CASE 1.—M. C., a thirty-three-year-old colored para x, was in the hospital from Feb. 3, 1931 until Mar. 4, 1931. She entered with a pressure of 190/115. Because of the borderline viability of the baby she was treated conservatively for twenty-five days when, because of increasing epigastric pain, headache and edema, a classical cesarean section was done and sterilization performed. The operation lasted forty-seven minutes, the postoperative condition was good. She had no postoperative convulsions.

Postmortem examination revealed: Generalized peritonitis, extreme fatty degeneration of the liver with no areas of focal necrosis; early arteriosclerosis and arteriosclerosis of the kidney with marked fatty degeneration, and early bronchopneumonia.

CASE 2.—A white primipara, thirty-four years of age, was sent into the hospital for observation Oct. 4, 1933 and delivered Oct. 18, 1933. She was first seen in the dispensary Sept. 5, 1933 and had no albuminuria or elevation of the blood pressure; on Sept. 18, 1933 she had a blood pressure of 152/102 and was advised as to diet and rest at home. At this time the urine showed a faint trace of albumin. On admission she was found to have a blood pressure of 166/104 and came into the hospital. On October 7 the blood chemistry showed nonprotein nitrogen 32, creatinine normal, and CO₂ combining power 48.

Following spontaneous labor and delivery she was apparently normal in every way. Three hours later she had a severe postpartum hemorrhage and went into shock. Stimulants were ordered, 1,500 c.c. of 5 per cent glucose and normal saline hypodermically caused a temporary improvement. She died in shock about fourteen hours after delivery.

The postmortem examination showed anemia of the parenchymatous organs, hemorrhage into the trachea and bronchi, petechial hemorrhages into the renal pelvis, generalized arteriosclerosis, fibrous adhesions of the pleura, and adenoma of the pancreas.

Microscopically the kidney findings were those of a toxic nephritis.

The liver findings showed no areas of thrombosis or necrosis.

Since similar cases clinically have shown hypoglycemia, blood was taken at autopsy which showed a glucose reading of 140 mg. per 100 c.c.

SUMMARY

The analysis of these cases serves to bring out certain points for consideration in connection with the etiology and treatment of this disease. Solomons has rightly said that if theories are to be of any use they must assist in determining suitable clinical treatment. We might go further and say that if a treatment based on a theory results in the marked reduction of the incidence, mortality, and morbidity of the disease, it helps to prove the correctness of the theory.

It is a significant fact that in Chicago in the same general grade of patient, with about the same type of hospital care, the mortality on the north side of Polk Street is between 16 and 20 per cent in the convulsive group, and on the south side of the street in the same block, there is no mortality in the same group. This is not due to superior knowledge or skill of the attending staffs of the two institutions, but to the smaller number of cases affording closer supervision and more attention to detail of management in the second institution, both before and after entry into the hospital.

That the mortality in a group of toxic women by careful handling can be brought down to the figure for pregnant women in general in well-conducted clinics is thought-provoking.

The fact that a disease which has for years held a mortality of from 20 to 30 per cent can be so controlled that there are not enough cases of the convulsive type in from twelve to fourteen hundred patients a year to demonstrate to the student convulsions or patients who have had convulsions, is important, especially when we remember that this type of intoxication is one of the most important of the causes of maternal mortality in the United States today.

Finally, it is important to note that this reduction in mortality and in the incidence of the convulsive stage of the disease is decreasing not only in one clinic but all over the country where adequate prenatal care is given.

There is, therefore, no excuse for the development of serious eclamptogenic toxemia except the ignorance or slothfulness of the physician and patient in applying what is already known to the control of the disease.

It is our duty to continually reiterate these facts to our students, to the medical profession, and to the laity, to the end, that this preventable malady will cease to take its annual toll.

CONCLUSIONS

1. Eclamptogenic toxemia can be controlled in most cases by reducing the amount of protein split products in the blood and increasing elimination by the bowel.
2. When the symptoms do not yield to conservative management, the uterus must be emptied.
3. Cesarean section is indicated in patients with fulminating toxemia or when induction of labor or delivery from below is contra-indicated.
4. Eyeground examination is of little value as an aid in determining the severity of a given case.
5. The phenolsulphonephthalein test is of value prognostically.

6. Treatment should be continued postpartum until the symptoms have definitely improved to reduce the incidence and severity of postpartum convulsions.

7. Sedatives, intravenous magnesium sulphate injections, and intravenous glucose injections, while rational and in some cases helpful, are not essential as part of the antepartum treatment.

8. Patients first seen in labor are usually best delivered from below.

9. Elderly primiparas near term but not in labor are best delivered by cesarean section because of the danger and uncertainty of delivery by induction of labor.

10. There is no advantage in dividing these cases into eclampsia, low reserve kidney, preeclampsias, and eclampsism.

11. Because of the prematurity and toxic condition of the babies in these cases extra precautions must be taken to insure their safety during labor and in the first days thereafter.

REFERENCES

- (1) *Falls, F. H.*: California & West. Med. 31: 1929. (2) *Solomons*: Trans. Am. Assn. Obst. & Gynec. 45: 10, 1932. (3) *Falls, F. H.*: J. A. M. A. 64: 1898, 1915. (4) *Hofbauer, J.*: AM. J. OBST. & GYNEC. 26: 311, 1933. (5) *Paramore*: Lancet 3: 11, 1928. (6) *Alvarez*: Physiol. Rev. 4: 352, 1924. (7) *Williams*: Obstetrics, New York, 1930, D. Appleton & Company, p. 668. (8) *Titus, Paul*: Trans. Am. Assn. Obst. & Gynec. & Abd. Surg. 60: 131, 1927. (9) *Williams*: Obstetrics, New York, 1933, D. Appleton & Company. (10) *DeLee*: Principles and Practice of Obstetrics, Philadelphia, 1920, W. B. Saunders Co., p. 378. (11) *Young, Jas.*: J. Obst. & Gynec. Brit. Emp., 1927. (12) *Falls and Moore*: J. A. M. A. 67: 574, 1916.

30 NORTH MICHIGAN AVENUE

Klaften, E.: The Treatment of Leukorrhea and Erosions by Vaginal Application of Insulin, Med. Klin. 50: 571, 1934.

During the last few years Klaften has been treating erosions of the cervix, ulcerations of the vagina and intractable leucorrhea by means of the local application of insulin. The author compared two series of cases of cervical erosion. In one he injected insulin hypodermically daily and in the other he applied insulin locally. Both series of women were on a high carbohydrate diet and in both series the cervical erosions cleared up. In diabetic women with cervical erosion, leucorrhea and pruritus of the vulva, improvement or cure was obtained in ten to fourteen days. The disappearance of the vaginal discharge runs parallel with the improvement in the diabetes and in some cases, return of the vaginal discharge was a forerunner of aggravation of the diabetic condition. Good results were also obtained in cases of nonspecific vaginitis and leucorrhea. This was especially apparent in cases where the customary local treatment failed to bring about improvement. In addition to the local applications of insulin, the patients were placed on a high carbohydrate diet and abundant calcium.

The good effects of insulin are due partly to the absorption of insulin into the general system and partly to the local effect which induces an increase in the glycogen content of the vaginal epithelium. The vaginal flora, however, is not affected by insulin.

J. P. GREENHILL.

FIVE-YEAR RESULTS IN FIFTY-SIX CASES OF CARCINOMA OF CORPUS UTERI*

QUITMAN U. NEWELL, M.D., F.A.C.S., AND
HARRY S. CROSSEN, M.D., F.A.C.S., ST. LOUIS, MO.

(From the Department of Obstetrics and Gynecology, Washington University School of Medicine and Barnes Hospital)

FROM Jan. 1, 1921, to Sept. 30, 1929, 56 patients with corpus uteri carcinoma were treated by Dr. H. S. Crossen and myself. The series included our private and ward cases in the Gynecological Service of the Barnes Hospital and Washington University Medical School.

In analyzing this group of cases, we have followed closely, plans laid down by Healy and Cutler in 1930. In this work we have devoted especial attention to two problems: first, the relationship between histologic structure and prognosis and, second, the comparative value of radiation and operation in the treatment of these growths. It is our purpose, therefore, to study the various factors which influence the ultimate result, as a help in determining the treatment of choice of each histologic type of corpus carcinoma. Until recent years these cases have been classified simply as carcinoma of the corpus uteri, no attempt being made to separate the different grades of carcinoma.

In our analysis we have followed the classification of Mahle, later confirmed by Healy.

- Grade I Superficial papillary adenoma malignum
- Grade II Adenoma malignum
- Grade III Adenocarcinoma
- Grade IV Diffuse (anaplastic) carcinoma

Adenoma Malignum (Grade II).—Of fifteen patients belonging to this group treated five years or more ago (Tables II, III, IV) seven were treated by hysterectomy alone. Five are alive five to six years after treatment. Two are dead. One died on the fourth day following operation from peritonitis and the other one died on the tenth postoperative day from bronchopneumonia. Five patients were treated by combined hysterectomy and radiation. Three are alive five to ten years after treatment. One died one and one-half years after treatment from recurrent cancer and the other one was living four years after treatment but then was lost in follow-up, hence considered as dead, although she may be alive. Three patients were treated by radiation alone. None survived five years. Two died of cancer. Cause of one death unknown.

*Read at the Forty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., September 6, 7, and 8, 1934.

In this series all the slides showing grading as to type of growth were reviewed by Dr. O. H. Schwarz, who has taken special interest in these pathologic problems.

TABLE I. PAPILLARY ADENOMA MALIGNUM GRADE I

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	OPERATION AND DATE	MG. HR. RADIUM DATE GIVEN	SERIES X-RAY	ALIVE	DEAD	REMARKS
11	70	0	3 mo.	-----	2400 8/6/23	2	11 yr.		Uterus normal size. 8/1/34 no cancer.
24	33	0	5 mo.	Complete hysterect. 4/7/25	None	1	9 yr.		Curettings showed sup. pap? adenoma malignum. 8/1/34 no cancer.
26	49	4	2 yr.	Complete hysterect. 5/28/25	None	None	9 yr.		Uterus enlarged. 4/5/34 no cancer.
54	37	4	2 mo.	Supravag. hysterect. 8/20/29	None	1	5 yr.		Cancer was not suspected. Op. was for enlarged uterus. 7/1/34 no cancer.

TABLE II. ADENOMA MALIGNUM GRADE II. TREATED BY HYSTERECTOMY ALONE

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	OPERATION DATE	ALIVE	DEAD	REMARKS
32	58	3	2 mo.	8/12/26		4 days	Curettings showed adenoma malignum. Died four days after operation. Peritonitis.
43	60	0	1 yr.	3/23/28	6 yr.		No curettage. 4/6/24 no cancer.
45	48	4	2 mo.	6/19/28	6 yr.		Uterus enlarged. 7/1/34 no cancer.
46	49	3	3 mo.	8/ 6/28	6 yr.		Curettings showed adenoma malignum. 7/14/24 no cancer.
47	38	0	None	10/ 6/28	6 yr.		Uterus enlarged. Myoma and ad. malig. Sup. vag. hysterect. 9/1/34 no cancer.
48	60	0	6 mo.	10/24/28		10 days	Died ten days after operation of bronchopneumonia.
49	49	0	1 yr.	3/12/29	5 yr.		No curettage. 7/24/34 no cancer.

Adenocarcinoma (Grade III).—Of twenty-seven patients belonging to this group, treated five years or more ago (Tables V, VI, VII), six were treated by hysterectomy alone. Four have survived five to eleven years. Two were lost in the follow-up and considered as dead. Fourteen patients were treated by combined hysterectomy and radiation. Nine are alive five to thirteen years after treatment. Five died within three years after treatment, four from cancer and one committed suicide because she had cancer. Seven patients were treated by radiation alone. One has survived five years and six died within four years after treatment.

Diffuse (Anaplastic) Carcinoma (Grade IV).—Of ten patients belonging to this group, treated five years or more ago (Table VIII), three are living six to eight years after treatment. Two were treated by combined hysterectomy and radiation and one by vaginal hysterectomy alone. Seven are dead, one died from postoperative

TABLE III. ADENOMA MALIGNUM GRADE II. TREATED BY COMBINED HYSTERECTOMY AND RADIATION

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	OPERATION DATE	MG. HR. RADIUM DATE GIVEN	SERIES X-RAY	ALIVE	DEAD	REMARKS
7	51	1	1 mo.	11/14/21	None	1	6 yr.		Curettings showed adenoma malignum. Died 8/24/27, cause not cancer.
16	55	0	2 mo.	8/12/24	None	3	10 yr.		Myoma and adenoma malignum. Cancer not suspected. Sup. vag. hysterect. 7/1/34 no cancer.
30	54	2	6 mo.	10/ 3/25	None	3		1½ yr.	Died of recurrent cancer April, 1927.
35	49	0	1 yr.	12/ 3/26	1600 11/26/26	None	5 yr.		Uterus enlarged. Curettings showed adenoma malignum. 3/2/32 no cancer.
52	53	0	2 yr.	4/29/29	None	1		4 yr. ?	Cancer not suspected. Operation was for myoma. 1/1/31 no cancer.

TABLE IV. ADENOMA MALIGNUM GRADE II. TREATED BY RADIATION ALONE

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	MG. HR. RADIUM DATE GIVEN INTRA-UTERINE	SERIES X-RAY	ALIVE	DEAD	REMARKS
15	60	3	2 yr.	3000 6/23/24	4		3 yr.	Enlarged uterus. Curettings showed Ad. Mal. Died 8/6/27, cause unknown. Last exam. 1927 no cancer.
36	42	3	3 yr.	3000 12/ 9/26	3		10 mo.	Enlarged uterus. Far advanced cancer. Died 8/23/27 of cancer.
51	48	0	1 yr.	3600 4/11/29 2500 7/ 2/32	2		3½ yr.	Large mass protruding from uterine canal. Ad. malignum. Cancer present 3 yr. after first radium. 8/24/32 last information. Probably died of cancer.

TABLE V. ADENOCARCINOMA GRADE III. TREATED BY HYSTERECTOMY ALONE

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	OPERATION DATE	ALIVE	DEAD	REMARKS
2	58	2	6 mo.	4/ 9/21	11 yr.		Curettings showed adenocarcinoma. 9/1/32 no cancer.
9	41	4	2 yr.	4/26/23	11 yr.		Enlarged uterus. Myomas and adenocarcinoma. 8/1/34 no cancer.
10	58	2	8 mo.	8/ 4/23		?	Lost in follow-up. Never returned after operation.
22	54	6	1 yr.	2/20/25	9 yr.		Curettings showed adenocarcinoma. 3/3/34 no cancer.
39	63	3	2 yr.	6/21/27		?	Lost in follow-up. Never returned after operation.
53	50	0	1 yr.	5/30/29	5 yr.		Enlarged uterus. Myoma and adenocarcinoma. 7/1/34 no cancer.

pneumonia on the fifth day following operation, and six died from cancer within one and one-half years after treatment. All of these cases were far-advanced carcinoma and the treatment given was mostly palliative.

Age Incidence.—The following is the distribution of corpus uteri carcinoma according to age: thirty to forty years, 4 cases; forty to fifty years, 15 cases; fifty to sixty years, 21 cases; sixty to seventy years, 13 cases; seventy to eighty years, 2 cases; eighty to ninety years, 1 case. The greatest number of cases occurred between the ages of fifty and sixty years. The second decade having most cases was forty to fifty years, and the third was sixty to seventy years. The youngest patient in our series was thirty-three years of age, and the oldest was eighty-one years of age.

Effect of Gestation.—Twenty of the patients were nulliparas, 4 were primiparas, 28 were multiparas, and 4 were unclassified.

Symptoms.—The average duration of symptoms in the entire series from time of onset to time of admission was twelve months. The outstanding clinical symptom is vaginal bleeding. Pain is a late manifestation of the disease.

CONCLUSIONS

The final discussion as to which is the best method of treatment for each of the several grades of carcinoma of the corpus must rest upon a large accumulation of reliably reported five-year results with the various methods. This detailed report is a contribution to such necessary accumulation. An additional item which should be included in such reports, is an accurate statement of the extent of the gross pathology in the specimen removed at operation. In this early series such information was lacking in a considerable proportion of the cases, but in later cases the gross findings in the specimen are recorded in detail, along with the microscopic findings. Such recording of the extent of the lesions in the structures removed, along with an accurate description of the clinical findings at examination and during operation or radium implantation, will enable more accurate classification of reported cases.

TABLE VI. ADENOCARCINOMA GRADE III. TREATED BY COMBINED HYSTERECTOMY AND RADIATION

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	OPERATION DATE	MG. HR. RADIUM DATE GIVEN	SERIES X-RAY	ALIVE	DEAD	REMARKS
4	58	3	1 yr.	10/ 1/21	None	1		2 mo.	Patient committed suicide shortly after being treated.
5	61	2	?	10/28/21	1125 10/ 2/21	None	7 yr.		Enlarged uterus. Curettings showed adenocarcinoma. 9/27/28 no cancer.
6	54	0	3 yr.	11/ 3/21	1200 10/26/21	None	13 yr.		Enlarged uterus. Curettings adenocarcinoma. 7/1/34 no cancer.
12	46	3	8 mo.	11/14/23	1745 9/12/23 1453 9/18/23	None	5 yr.		Curettings adenocarcinoma. Uterus removed showed no cancer. 10/10/28 no cancer.
14	44	0	1 yr.	1/ 3/24	None	3		3 yr.	Myoma and adenocarcinoma. 1927 died of cancer.
18	53	0	3 yr.	7/30/24	None	2	5 yr.		Curettings adenocarcinoma. 5/27/29 no of cancer.
19	62	3	5 mo.	8/14/24	None	1	10 yr.		Enlarged uterus. Curettings adenocarcinoma. 9/1/34 no cancer.
23	58	0	?	4/ 4/25	None	1		1 yr.	Curettings adenocarcinoma. Enlarged uterus. 9/8/26 died of cancer.
25	48	0	6 mo.	4/24/25	None	2		1 yr.	Uterus small. Curettings adenocarcinoma. 5/24/26 died of cancer.
28	69	3	5 mo.	8/13/25	None	1	9 yr.		Enlarged uterus. Curettings adenocarcinoma. 8/1/34 no cancer.
34	57	1	6 mo.	11/20/26	1800 10/28/26	None	8 yr.		Curettings adenocarcinoma. 4/23/34 no cancer.
40	76	0	2 yr.	11/23/27	None	1	6 yr.		Enlarged uterus. Curettings adenocarcinoma. 7/25/33 no cancer.
55	51	3	?	9/ 5/29	None	1		3 yr.	Myoma and adenocarcinoma. Cancer not suspect. 11/1/32 no cancer.
56	42	0	3 yr.	10/17/29	2400 9/ 1/29	2	5 yr.		Myoma and adenocarcinoma. Curettings adenocarcinoma. 7/1/34 no cancer.

TABLE VII. ADENOCARCINOMA GRADE III. TREATED BY RADIATION ALONE

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	MG. HR. RADIUM DATE GIVEN INTRA-UTERINE	SERIES X-RAY	ALIVE	DEAD	REMARKS
3	62	3	1 yr.	1350 6/27/21	2		4 mo.	Enlarged uterus. Advanced cancer. Last information 8/26/21 not well.
13	62	?	2 mo.	None	1 12/ 4/23		?	Advanced cancer. Curettings showed adenocarcinoma. Died shortly after treatment.
21	57	0	2 yr.	None	2 2/14/25		?	Advanced cancer. Curettings showed adenocarcinoma. Died shortly after treatment.
29	66	1	1 yr.	1800 9/ 7/25 1000 10/ 7/25	1		2 mo.	Advanced cancer with heart disease. Uterus large. 11/13/25 died of heart disease.
31	81	0	6 mo.	1000 11/21/25 2000 12/ 7/25	1		4 yr.	Curettings showed carcinoma. 7/6/29 died of senility.
41	56	2	1 yr.	None	1 12/23/27		2 yr.	Enlarged uterus. Advanced cancer. 1/13/30 died of cancer.
50	64	7	?	2500 4/ 6/29	2	5 yr.		Uterus small. Curettings showed adenocarcinoma. 4/30/34 no cancer.

In comparing the results of different methods of treatment for any grade of corpus carcinoma, the comparison should be made with cases of the same approximate extent, i.e., early cases to early cases and late cases to late cases. Otherwise there may be erroneous conclusions as to the efficacy of the different treatment methods. This point is illustrated by this series, in which death resulted in nearly all patients receiving only radiation treatment. Thus the general results would indicate that radiation has very little effect toward cure. But when the extent of the disease is looked into, we find that practically all cases presenting reasonable hope of cure were subjected to operation, radiation alone being limited to the hopeless cases. Hence the results do not show the relative efficacy of radiation even of those days, and much less of the improved radiation of the present.

Basing our decision on subsequent five years of experience along with the experience with the cases reported, we feel at present that operation plus radiation is the safest plan of treatment for carcinoma

TABLE III. ADENOMA MALIGNUM GRADE II. TREATED BY COMBINED HYSTERECTOMY AND RADIATION

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	OPERATION DATE	MG. HR. RADIUM DATE GIVEN	SERIES X-RAY	ALIVE	DEAD	REMARKS
7	51	1	1 mo.	11/14/21	None	1	6 yr.		Curettings showed adenoma malignum. Died 8/24/27, cause not cancer.
16	55	0	2 mo.	8/12/24	None	3	10 yr.		Myoma and adenoma malignum. Cancer not suspected. Sup. vag. hysterect. 7/1/34 no cancer.
30	54	2	6 mo.	10/ 3/25	None	3		1½ yr.	Died of recurrent cancer April, 1927.
35	49	0	1 yr.	12/ 3/26	1600 11/26/26	None	5 yr.		Uterus enlarged. Curettings showed adenoma malignum. 3/2/32 no cancer.
52	53	0	2 yr.	4/29/29	None	1		4 yr. ?	Cancer not suspected. Operation was for myoma. 1/1/31 no cancer.

TABLE IV. ADENOMA MALIGNUM GRADE II. TREATED BY RADIATION ALONE

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	MG. HR. RADIUM DATE GIVEN INTRA-UTERINE	SERIES X-RAY	ALIVE	DEAD	REMARKS
15	60	3	2 yr.	3000 6/23/24	4		3 yr.	Enlarged uterus. Curettings showed Ad. Mal. Died 8/6/27, cause unknown. Last exam. 1927 no cancer.
36	42	3	3 yr.	3000 12/ 9/26	3		10 mo.	Enlarged uterus. Far advanced cancer. Died 8/23/27 of cancer.
51	48	0	1 yr.	3600 4/11/29 2500 7/ 2/32	2		3½ yr.	Large mass protruding from uterine canal. Ad. malignum. Cancer present 3 yr. after first radium. 8/24/32 last information. Probably died of cancer.

TABLE V. ADENOCARCINOMA GRADE III. TREATED BY HYSTERECTOMY ALONE

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	OPERATION DATE	ALIVE	DEAD	REMARKS
2	58	2	6 mo.	4/ 9/21	11 yr.		Curettings showed adenocarcinoma. 9/1/32 no cancer.
9	41	4	2 yr.	4/26/23	11 yr.		Enlarged uterus. Myomas and adenocarcinoma. 8/1/34 no cancer.
10	58	2	8 mo.	8/ 4/23		?	Lost in follow-up. Never returned after operation.
22	54	6	1 yr.	2/20/25	9 yr.		Curettings showed adenocarcinoma. 3/3/34 no cancer.
39	63	3	2 yr.	6/21/27		?	Lost in follow-up. Never returned after operation.
53	50	0	1 yr.	5/30/29	5 yr.		Enlarged uterus. Myoma and adenocarcinoma. 7/1/34 no cancer.

pneumonia on the fifth day following operation, and six died from cancer within one and one-half years after treatment. All of these cases were far-advanced carcinoma and the treatment given was mostly palliative.

Age Incidence.—The following is the distribution of corpus uteri carcinoma according to age: thirty to forty years, 4 cases; forty to fifty years, 15 cases; fifty to sixty years, 21 cases; sixty to seventy years, 13 cases; seventy to eighty years, 2 cases; eighty to ninety years, 1 case. The greatest number of cases occurred between the ages of fifty and sixty years. The second decade having most cases was forty to fifty years, and the third was sixty to seventy years. The youngest patient in our series was thirty-three years of age, and the oldest was eighty-one years of age.

Effect of Gestation.—Twenty of the patients were nulliparas, 4 were primiparas, 28 were multiparas, and 4 were unclassified.

Symptoms.—The average duration of symptoms in the entire series from time of onset to time of admission was twelve months. The outstanding clinical symptom is vaginal bleeding. Pain is a late manifestation of the disease.

CONCLUSIONS

The final discussion as to which is the best method of treatment for each of the several grades of carcinoma of the corpus must rest upon a large accumulation of reliably reported five-year results with the various methods. This detailed report is a contribution to such necessary accumulation. An additional item which should be included in such reports, is an accurate statement of the extent of the gross pathology in the specimen removed at operation. In this early series such information was lacking in a considerable proportion of the cases, but in later cases the gross findings in the specimen are recorded in detail, along with the microscopic findings. Such recording of the extent of the lesions in the structures removed, along with an accurate description of the clinical findings at examination and during operation or radium implantation, will enable more accurate classification of reported cases.

TABLE VI. ADENOCARCINOMA GRADE III. TREATED BY COMBINED HYSTERECTOMY AND RADIATION

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	OPERATION DATE	MG. HR. RADIUM DATE GIVEN	SERIES X-RAY	ALIVE	DEAD	REMARKS
4	58	3	1 yr.	10/ 1/21	None	1		2 mo.	Patient committed suicide shortly after being treated.
5	61	2	?	10/28/21	1125 10/ 2/21	None	7 yr.		Enlarged uterus. Curettings showed adenocarcinoma. 9/27/28 no cancer.
6	54	0	3 yr.	11/ 3/21	1200 10/26/21	None	13 yr.		Enlarged uterus. Curettings adenocarcinoma. 7/1/34 no cancer.
12	46	3	8 mo.	11/14/23	1745 9/12/23 1453 9/18/23	None	5 yr.		Curettings adenocarcinoma. Uterus removed showed no cancer. 10/10/28 no cancer.
14	44	0	1 yr.	1/ 3/24	None	3		3 yr.	Myoma and adenocarcinoma. 1927 died of cancer.
18	53	0	3 yr.	7/30/24	None	2	5 yr.		Curettings adenocarcinoma. 5/27/29 no of cancer.
19	62	3	5 mo.	8/14/24	None	1	10 yr.		Enlarged uterus. Curettings adenocarcinoma. 9/1/34 no cancer.
23	58	0	?	4/ 4/25	None	1		1 yr.	Curettings adenocarcinoma. Enlarged uterus. 9/8/26 died of cancer.
25	48	0	6 mo.	4/24/25	None	2		1 yr.	Uterus small. Curettings adenocarcinoma. 5/24/26 died of cancer.
28	69	3	5 mo.	8/13/25	None	1	9 yr.		Enlarged uterus. Curettings adenocarcinoma. 8/1/34 no cancer.
34	57	1	6 mo.	11/20/26	1800 10/28/26	None	8 yr.		Curettings adenocarcinoma. 4/23/34 no cancer.
40	76	0	2 yr.	11/23/27	None	1	6 yr.		Enlarged uterus. Curettings adenocarcinoma. 7/25/33 no cancer.
55	51	3	?	9/ 5/29	None	1		3 yr.	Myoma and adenocarcinoma. Cancer not suspect. 11/1/32 no cancer.
56	42	0	3 yr.	10/17/29	2400 9/ 1/29	2	5 yr.		Myoma and adenocarcinoma. Curettings adenocarcinoma. 7/1/34 no cancer.

TABLE VII. ADENOCARCINOMA GRADE III. TREATED BY RADIATION ALONE

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	MG. HR. RADIUM DATE GIVEN INTRA-UTERINE	SERIES X-RAY	ALIVE	DEAD	REMARKS
3	62	3	1 yr.	1350 6/27/21	2		4 mo.	Enlarged uterus. Advanced cancer. Last information 8/26/21 not well.
13	62	?	2 mo.	None	1 12/ 4/23		?	Advanced cancer. Curettings showed adenocarcinoma. Died shortly after treatment.
21	57	0	2 yr.	None	2 2/14/25		?	Advanced cancer. Curettings showed adenocarcinoma. Died shortly after treatment.
29	66	1	1 yr.	1800 9/ 7/25 1000 10/ 7/25	1		2 mo.	Advanced cancer with heart disease. Uterus large. 11/13/25 died of heart disease.
31	81	0	6 mo.	1000 11/21/25 2000 12/ 7/25	1		4 yr.	Curettings showed carcinoma. 7/6/29 died of senility.
41	56	2	1 yr.	None	1 12/23/27		2 yr.	Enlarged uterus. Advanced cancer. 1/13/30 died of cancer.
50	64	7	?	2500 4/ 6/29	2	5 yr.		Uterus small. Curettings showed adenocarcinoma. 4/30/34 no cancer.

In comparing the results of different methods of treatment for any grade of corpus carcinoma, the comparison should be made with cases of the same approximate extent, i.e., early cases to early cases and late cases to late cases. Otherwise there may be erroneous conclusions as to the efficacy of the different treatment methods. This point is illustrated by this series, in which death resulted in nearly all patients receiving only radiation treatment. Thus the general results would indicate that radiation has very little effect toward cure. But when the extent of the disease is looked into, we find that practically all cases presenting reasonable hope of cure were subjected to operation, radiation alone being limited to the hopeless cases. Hence the results do not show the relative efficacy of radiation even of those days, and much less of the improved radiation of the present.

Basing our decision on subsequent five years of experience along with the experience with the cases reported, we feel at present that operation plus radiation is the safest plan of treatment for carcinoma

TABLE VIII. DIFFUSE (ANAPLASTIC) CARCINOMA GROUP IV

CASE	AGE	NO. PREG.	DURATION SYMPTOMS	OPERATION AND DATE	MG. HR. RADIUM DATE GIVEN	SERIES X-RAY	ALIVE	DEAD	REMARKS
1	38	2	3 yr.	Supravag. hysterect. 1/9/21	None	None		1 mo.	Far advanced cancer. Feb., 1921, died of cancer.
8	64	7	1 yr.	Explorat. lap.	1800 4/ 1/22	None		?	Advanced cancer. Died shortly after treatment.
17	57	1	1 yr.	None	3000 7/ 5/24	None		13 days	Advanced cancer. 7/18/24 died of cancer.
20	61	5	2 yr.	None	3000 11/ 3/24	2		1 yr.	Curettings cancer. 11/13/25 died of cancer.
27	48	?	1 yr.	Supravag. hysterect. 8/1/25	2000 7/ 6/25	1		1½ yr.	Curettings cancer. Received some radium elsewhere. 2/17/27 died of cancer.
33	43	?	?	Supravag. hysterect. 9/1/26	None	None		5 days	Cancer not suspected at time of operation. 9/6/26, died of pneumonia.
37	57	3	3 yr.	Vaginal hysterect. 12/17/26	None	None	8 yr.		Cancer not suspected at time of operation. 9/1/34, no cancer.
38	56	11	1 yr.	Supravag. hysterect. 3/10/27	None	None		?	Enlarged uterus. Died shortly after operation.
42	54	0	4 mo.	Complete hysterect. 12/23/27	None	2	6 yr.		Enlarged uterus. Inoperable. 9/28/33, died of cancer.
44	61	3	1 mo.	Complete hysterect. 5/24/28	None	1	6 yr.		Curettings cancer. 9/1/34, no cancer.

TABLE IX. NUMBER OF FIVE-YEAR CURES IN DIFFERENT GRADES BY DIFFERENT TREATMENTS

	HYSTERECTOMY ALONE					HYSTERECTOMY AND RADIATION COMBINED					RADIATION ALONE					TOTAL TREATED 5 YEARS AGO
	GRADE I	GRADE II	GRADE III	GRADE IV	TOTAL	GRADE I	GRADE II	GRADE III	GRADE IV	TOTAL	GRADE I	GRADE II	GRADE III	GRADE IV	TOTAL	
Number patients treated 5 yr. ago	3	7	6	4	20		5	14	4	23	1	3	7	2	13	56
Alive 5 to 13 years after treatment	3	5	4	1	13		3	9	2	14	1		1		2	29
Died after treatment		2		3	5		2	5	2	9		3	6	2	11	25
Lost, unable to locate			2	0	2				0	0						2
Total	3	7	6	4	20		5	14	4	23	1	3	7	2	13	56

of the corpus uteri. If the patient is a good operative risk, hysterectomy of a type suitable for this disease is carried out. Such hysterectomy is supplemented by radiation to devitalize any cancer cells which may be beyond the structures removed. This may be given before or after the operation or both, and may be given by means of radium or x-ray or both. If the patient is a poor operative risk, the treatment to be employed is determined by a careful consideration of the seriousness of the contraindication to operation and of the efficacy of radiation in a growth of that particular type and extent.

WALL BUILDING

INTRACTABLE DYSMENORRHEA*

RELIEF BY SYMPATHETIC NEURECTOMY

FREDERICK S. WETHERELL, M.D., F.A.C.S., SYRACUSE, N. Y.

(From the Gynecological Service of St. Joseph Hospital)

QUI *dolorem vincit, humanitati servit*. The recent developments in sympathetic nerve surgery in its relation to relief of pain have given us added opportunities to serve humanity in this respect. The relief afforded women suffering from dysmenorrhea following excision of the superior hypogastric sympathetic nerve plexus (presacral nerve) seems to indicate, when compared with the amelioration of pain afforded in other conditions which cause pelvic pain, that it is in dysmenorrhea that sympathectomy will be of outstanding value. This statement is made as a result of personal observations, and recent reports by American colleagues.¹ The experience in this country closely parallels that of European surgeons.

The anatomy and technical surgical procedure has been so well and repeatedly described in recent literature,² both in this country and abroad, that only a brief summary is here presented, including a discussion of technical points to be observed. I have operated upon three women with primary (spasmodic) dysmenorrhea, and upon several in whom there was a mild dysmenorrhea (secondary, congestive type), in whom the operation was done as an added procedure during the course of other pelvic work. Although the latter group of patients have had comfortable menstrual periods since the operation, I am reporting here only the three patients in whom the operation was performed primarily for the relief of dysmenorrhea of a severe type. One of these women has since had a baby. Her obstetric history is given in detail.

*Read at the Forty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., September 6, 7, and 8, 1934.

Recent reports in American literature indicate that the operation has been done rather extensively, and that there is always a mortality rate in abdominal operations, even though it be low, must be kept in mind. It is for that reason that I feel the operation should be limited to the more severe types of dysmenorrhea. Of course, if at the insistence of the patient, and because of the individual patient's unstable nervous system, with the resultant magnification of symptoms plus the inevitable economic features such as loss of position, disturbance of familial relationship, etc., one may be forced to accept the risk.

Severe dysmenorrhea has until recently, and as a last resort, been treated by either hysterectomy, radiation therapy, or opiates. Section of the sympathetic plexus has had no deleterious after-effects, which might militate against employing this procedure in young women, when the operation is properly performed. There has been no difference in libido, nor has it interfered with subsequent pregnancy or delivery. When considered in this light it must appeal to the gynecologist as a method preferable to anything which has been at his command before sympathectomy was promulgated as a relief measure.

TYPES OF DYSMENORRHEA TREATED

The terms "primary" or "spasmodic," and "secondary" or "congestive," "dysmenorrhea," are made use of in this discussion. By the former we mean that condition in which there is an entire absence of gross pathologic lesions in the pelvis, and in which the pain begins just before or with the appearance of menstruation; and the second in which there is some gross pathologic lesion accompanying the menstrual disturbance and in which the discomfort begins some days before the beginning of the period. The pain in the former group is in the majority of cases much more severe and more disabling than in the latter.

Practically everything in the armamentarium of the gynecologist has been tried for the relief of primary dysmenorrhea, and many theories have been advanced as to its cause. The multiplicity of drugs, and formerly, the numerous operations performed for the relief of dysmenorrhea, is evidence of lack of specificity. This is also true in the matter of the endocrines, for although some cases have responded for a time, many of these patients have eventually had a recurrence of symptoms. The hypoplastic, underdeveloped uterus may be a factor in the etiology because of the disturbed circulation at the time of menstruation. As shown in Case 3 there is a definite possibility that sectioning of the sympathetic nervous supply may improve the circulation, and secondarily cause an increase in the size of the uterus.

The antispasmodic effect of atropine is well known, and it should be remembered that this result is achieved by action on the sympathetic nervous system. Atropine, too, has been our most useful drug in the treatment of dysmenorrhea. This point is interesting because of the fact that the operation under discussion severs most of the sympathetic nerves in connection with the uterus. That pain impulses are conducted through the superior hypogastric plexus is a well-recognized fact. Sectioning of these fibers, therefore, should relieve pain emanating from the uterus whether it be the result of muscle spasm or arterial contractions. Vasospasm *per se* causes pain. Sympathetic nerve sectioning relieves this spasm in peripheral arterial disease, and if such spasm is a factor in dysmenorrhea, some of the relief might be explained on this basis.

It might be that we are seeking a cause in the uterus itself; whereas, it may be quite possible that incident to the congestion accompanying menstruation, there is a stimulation of hypersensitive nerve fibers, some of which may be directly concerned with the conduction of pain impulses.³ The development of such an hypothesis has interesting possibilities relative to the further study of etiologic factors. In only one case did the pathologist report evidence of inflammatory change in the nerve tissue. This of course might be a factor, and might be discovered only by careful serial sectioning of the entire plexus. It must be kept in mind, however, that sympathetic nervous systems vary as do individuals, and one system might be more prone to react to slight insults than another. Most women with dysmenorrhea fall into the group of "sympathetico-tonics," which adds interest to the speculation that we may be dealing with a disturbance of normal balance, with a hypersensitive uterine sympathetic nervous mechanism, and that agitation of the same at the menstrual period, eventuates in painful overactivity.

ANATOMY AND OPERATION

The surgical anatomy of the so-called presacral nerve, better known as the superior hypogastric plexus (it does not lie in front of the sacrum), has been well described by Elaut,⁴ Cotte,² and Fountaine⁵ have discussed the operation, the former having developed the technic as it stands today.

The completeness of the contributions of these men make it unnecessary to do more than briefly recall a few salient points.

The superior hypogastric plexus lies in a region quite familiar to the pelvic surgeon. He needs but to pick up the posterior parietal peritoneum overlying the triangle formed by the bifurcation of the aorta, incise this layer, and thus find the area containing the plexus. In some cases the mesosigmoid is implanted to the right of the midline. This adds difficulty to the procedure, for vessels must be spared. In these cases I have found that a small nick in the right leaf, followed

by gentle tearing of the peritoneum is of great assistance in the avoidance of vessel injury. In the ordinary case, of course, a longitudinal incision is made with the scissors. This should extend about an inch above the bifurcation of the aorta, and downward to the level of the sacral promontory. A long peritoneal incision facilitates retraction laterally, and materially aids exposure. Repeatedly drying the area with a gauze sponge aids in the definition of the finer strands, which are often no larger than a thread in a spider web. This is particularly true in the lateral areas, where communicating fibers from the intersigmoid plexus, and from the lower lumbar sympathetic chain are to be found. It is quite likely that failure to pick up some of these small fibers has been the reason for a few reports of unsatisfactory results.

At the lower end of the plexus two distinct bundles of nerve fibers may be seen: the hypogastric nerves. It is here that care must be exercised. When cutting through the lower plexus fibers, no part of these bundles should be included, for it is quite likely that inclusion of extensive pieces of the hypogastric nerves may be the cause of bladder disturbances.

The usual midline incision is made but may well be extended for a short distance above and to the left of the umbilicus. The bowel should be well emptied by saline enemas, thus materially aiding the necessary "packing away" of the intestines, so essential to good exposure of the area attacked. Spinal anesthesia aids materially in this essential. The fibers of the plexus are best picked up by means of a small blunt hook. Palpation of the two common iliac arteries at the bifurcation of the aorta materially assists in the location of the area, and indicates the point where the fibers are most readily seen. A small dental cotton pledget on a long forcep or hemostat is a useful instrument for teasing out the fibers. Fibers should be definitely identified. Often the main group of strands lies close to, or even slightly under, the left common iliac artery, and this must be kept in mind if a complete dissection is to be made.

CASE HISTORIES

CASE 1.—Mrs. F. M., aged twenty-five, occupation, office clerk. Her chief complaint was severe dysmenorrhea since the beginning of menstruation at the age of thirteen, and dyspareunia since her marriage in August, 1933. She had regular twenty-eight-day periods of four days' duration. Cramps always began about two hours before the beginning of the menstrual flow, and were of terrific severity for four hours, after which the patient was exhausted. Her lower abdomen remained sore for five days, and she was unable to work during that time. Vomiting occurred synchronously with the cramps. Her general health had been good and she had never had a serious illness. All the usual medical treatments had been of no avail. Physical examination disclosed a well-nourished young woman with no evidence of pathologic conditions. It was difficult to examine her vaginally as the introitus was small, and extremely sensitive. She was very anxious for relief, for she was in danger of losing her position as the result of repeated absence from work.

She was operated upon April 30, 1934, at which time the uterus was found to be normal in size, and the ovaries and tubes normal. There were no adhesions in the pelvis. The appendix was tightly bound down in a retrocecal position, and was removed with some difficulty. The superior hypogastric sympathetic nerve plexus was then excised.

One week after the operation the patient menstruated and had absolutely no pelvic discomfort. Quite naturally, she was delighted, and it was the first time

during her menstrual life that this had occurred. Her postoperative course was entirely uneventful. Recent follow-up shows that this relief has continued, and she loses no time from work. There is no dyspareunia.

CASE 2.—Mrs. A. E. H., aged twenty-three, stenographer. Began menstruating at the age of twelve, and continued to menstruate at five-week intervals until a few months before the present examination on June 9, 1933, at which time she began menstruating every twenty-eight days and had five-day periods of a moderate amount. She had always had severe cramps for about two hours, at the beginning of each period. In 1931 she was practically free from dysmenorrhea, but in the middle of 1932 the cramps, which had begun early in the year, became increasingly severe until, as she described it, she was in agony all of the first day and usually had to stay in bed about three days. The pains, however, lasted for the entire five-day period. There had been no previous serious illnesses. It was interesting to note that her mother died of apoplexy at fifty-two, and that she had also suffered from dysmenorrhea. This patient had employed several physicians, and had been given all of the usual medical care without benefit. She finally employed an osteopath, and then at the end, a chiropractor. She was in great danger of losing her position.

At operation no pathologic condition was found in the pelvis. The superior hypogastric plexus was resected under spinal anesthesia. Following the operation there was difficulty in urinating, and it was necessary to catheterize her for about three days. Then for about three days she had a marked urinary frequency. This gradually disappeared and bladder function was normal in ten days. She had always been constipated and was in the habit of taking cathartics. Following her operation her constipation gradually disappeared until, at the present time, her bowels move normally. This effect is in keeping with the results reported in relation to the relief of constipation in individuals whose superior hypogastric plexus had been removed for the cure of that condition. The first period after the operation occurred in five weeks. This delay upset her somewhat and, as she stated when her menstruation began, she had a tingling sensation in both hip regions which made her fear that she was going to have cramps so she went to bed. No cramps occurring, however, she got up and did a half day's baking. Since then she has had a disturbing backache at the time of her periods, but no pelvic pain, and is able to continue with her work. She had been told that the operation would cause frigidity. This, she states, has not occurred.

CASE 3.—Mrs. P. L., aged twenty-six, a nurse. This case has been previously reported in the *Journal of the American Medical Association* (101: 1295, 1933). An error occurred in the case history as then reported, and should be noted at this time. It was stated that, "the uterus was normal in size," whereas it should have read, "the uterus was subnormal in size." This woman had had dysmenorrhea since she began to menstruate at the age of fourteen. Her periods had always been scanty, and for the two years preceding the time that she consulted me, there had been a gradual increase in the severity of her dysmenorrhea. She was unable to work, sometimes for two weeks, the disturbance toward the end having made it necessary for her to stay in bed nearly three weeks. She was very obese, being eighty pounds overweight. No medical treatment was of avail, and her physician at times had to resort to morphine. As previously reported, both ovaries were markedly sclerotic and the left one was removed, the right one being partially resected, a piece approximately one inch long, one-half inch wide, and one-quarter inch thick being left along the hilus. This patient menstruated regularly and without pain until thirteen months after her operation. She was sent to me in May,

1934, more than a year and a half later. Her physician felt that she might have a large ovarian cyst, or that she was pregnant. A diagnosis of pregnancy was made.

She was delivered of a living child on Aug. 15, 1934. Her first stage was conducted under morphine and scopolamine and lasted approximately eighteen hours. The pains were irregular and weak, and were mostly in the nature of a backache. She had no pains in front. The position was right occiput posterior. Her second stage lasted between four and five hours, and the head rotated to an occiput posterior position. Her physician (Dr. E. J. Dillon, Phoenix, N. Y.), called in an obstetrician (Dr. R. J. Pieri, Syracuse, N. Y.), who found that the head was not down on the perineum. Under ether anesthesia a Scanzoni midforceps operation was performed. Both physicians noted the unusual relaxation of the perineum, and the obstetrician found it unnecessary to iron out the perineum. The babe weighed 8½ pounds. The patient made a perfect recovery following delivery. This case is interesting from several standpoints: first, the period of sterility during her four years of married life; second, the hypoplastic, underdeveloped uterus; third, the labor pains during the first stage, which were observed by her physician throughout the period. While merely conjecture, it is nevertheless interesting to speculate on the effect of section of the sympathetic nerve supply and its relation to increased nourishment secondary to vasodilatation of the uterine vessels. This case shows well the conservative nature of the operation, in that complete ovarian function was preserved even though only a small slice of ovary remained. Not long ago either radiation or hysterectomy would have been employed in this case, for the condition of the patient was pitiful. It also answers well the question which has often been asked as to the effect on pregnancy. Other authors have stated that childbearing was not interfered with and the only effect noted was that low forceps delivery was demanded more than usual.

RESULTS

In Case 1 the relief of symptoms was complete, but in the other two there was a complaint of backache and a feeling of discomfort in both hip regions. It is easy to conceive that with relief from the extremely severe cramps, the other aches would be more noticeable. Inasmuch as there are nerve fibers from the parasympathetic sacral outflow, and a few of the ovarian plexus fibers in relation to the main uterine sympathetic supply, these residual symptoms can be easily explained.

The occasional bladder symptoms are very likely due to interference with fibers of the sympathetic and parasympathetic supply to that organ. This may in large part be avoided by guarding against too low an incision of the plexus, i. e., by sectioning only fibers of the superior hypogastric plexus at the lower end, thus sparing the fibers of the hypogastric nerves with their lateral parasympathetic connections. A temporary upset of the bladder nervous mechanism as a result of surgical interference, even when correctly applied, may also be a factor, but the disturbance should be transient.

As stated by Kuntz, the uterine plexus has direct connection with the lower lumbar chain ganglia, lying alongside the lumbar vertebrae. Careful search at the origin of the common iliac arteries will disclose

fine fibers crossing the same. These fibers originate in the lumbar chain and if not severed, may be the cause of residual ache in the distribution of the lower thoracic and upper lumbar spinal nerves.

CONCLUSIONS

The operation of resection of the superior hypogastric plexus of sympathetic nerves for the relief of dysmenorrhea, rightly belongs in the domain of the gynecologist; one who is able to analyze the individual case and to determine whether everything has been done in a medical way for the relief of the dysmenorrhea. Furthermore, it is necessary that he be able to judge the necessity for removal of gross pathologic conditions if found present. It is not merely a question of whether the surgeon is able to resect the plexus, but whether the individual case has been fairly studied and that nothing remains to afford relief except surgery. In the light of previous radical treatment, such as radiation, hysterectomy, or the use of opiates, the operation here discussed is a conservative one, but the ever present possibility of a mortality must be kept in mind and the operation advised only in those cases in which there is definite evidence that no treatment other than the previously mentioned radical procedures, is of avail. Furthermore, the operator's experience should be such, that in cases of secondary dysmenorrhea requiring other surgery, the operation will be performed with such rapidity as will allow enough time for the added nerve resection without jeopardizing the patient's chances.

There is no deleterious effect on libido, or future pregnancy, because of resection of the superior hypogastric plexus.

REFERENCES

- (1) *Adson, A. W., and Masson, J. C.*: J. A. M. A. 102: 987, 1934. (2) *Cotte, G.*: Presse méd. 30: 98, 1925. (3) *Heinbecker, Peter*: J. Thoracic Surg. 2: 183, 1932. (4) *Elaut, L.*: Surg. Gynec. Obst. 55: 581, 1932. (5) *Fontaine, R., and Herrmann, L. G.*: Surg. Gynec. Obst. 54: 133, 1932. (6) *Kuntz, A.*: Autonomic Nervous System, Philadelphia, 1929, Lea and Febiger, p. 304. (7) *Dahl, W.*: Ztschr. f. d. Geburtsh. u. Gynäk. 78: 539, 1916.

713 EAST GENESEE STREET

Young, A. M.: Five Hundred and Nineteen Vogt Bromine Tests of Urine for Pregnancy, J. Lab. & Clin. Med. 19: 153, 1933.

The author, in a series of 519 specimens, has shown that the Vogt bromine test (slightly modified) is far from satisfactory for the diagnosis or exclusion of pregnancy. Positive results were obtained in 63 per cent of pregnancy urines and negative results in only 84 per cent of the nonpregnancy urines. The Vogt test, briefly, is a color test for histamine or histidine with a bromine reagent.

The Aschheim-Zondek and Friedman tests are well known and accurate, yet they require the use of mice or rabbits, are expensive and time-consuming, thus there is a need for a simple chemical test.

W. B. SERBIN.

PNEUMOCOCCUS PELVIC INFECTION IN ADULTS*

JAMES E. KING, M.D., BUFFALO, N. Y.

INFECTION of the peritoneal cavity by the pneumococcus was brought to the attention of the profession by Bozzolo in 1885. Since that time sporadic reports of such cases have appeared in the literature. The first reports were concerned with the disease in children and the pediatricians soon recognized it as a clinical entity. Most of the published reports, however, are by surgeons whose surgical attack upon these cases afforded opportunities for clinical, bacteriologic, and pathologic study.

These early reports indicated that the condition occurred only in female children. As late as 1925 Gibson¹ stated that the so-called primary type was seen only in young girls. Wolfsohn,² however, in that same year reported before the Berliner Medizinische Gesellschaft a few similar cases occurring in males. There also began to appear reports of scattered cases occurring in adult females. A study of these adult cases indicates that a large majority have an especial interest for the gynecologist and obstetrician. This relationship is apparent in the following three cases occurring in my practice:

CASE 1.—Mrs. R. S., aged forty-two years, had always been well; three children, youngest 4 years, miscarriage one and one-half years before present illness. Admitted Dec. 28, 1932. Illness began with sudden onset Dec. 23, 1932, with a chill, rise of temperature and pains in her back and bones. A physician who was called diagnosed "Flu." At this time there was no abdominal pain. She did notice, however, a vaginal discharge, thin, purulent, and odorless. December 24: No improvement in general condition but still no abdominal pain. December 25: Had severe chill and developed cramp-like pains in lower abdomen and back. December 26 to 27: Increase in abdominal pains especially below the umbilicus. Some diarrhea, believed to be due to a cathartic she had taken. Bowel movements painful. On the twenty-seventh, had definite pain in right shoulder. Was admitted to the hospital on the morning of the twenty-eighth acutely ill. Temperature 103° F., pulse 100. Examination on admission showed abdomen to be distended with moderate muscle rigidity. Marked tenderness of lower abdomen especially at the left. Cervix somewhat anterior with painful swelling posteriorly and laterally. Vaginal discharge present. White cell count 26,800, polynuclears 90 per cent. Diagnosis: Beginning pelvic abscess. On the twenty-ninth cervix found pushed high behind the symphysis, due to a marked increase of the mass posteriorly. Immediate colpotomy decided upon. Before opening the vagina swabs were taken from the uterus. Incision behind the cervix evacuated large quantity of odorless, flaked pus. Specimen collected for study. Following this the temperature fell to normal on the

*Read at the Forty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, White Sulphur Springs, W. Va., September 6, 7, and 8, 1934.

sixth day, and the patient was discharged on the tenth day following operation. The smears and cultures from the uterus showed pneumococcus Type IV. Verified by mouse inoculation. Pus from abscess showed same organism. Blood culture on January 2 negative.

CASE 2.—Mrs. S. H., aged forty-six, married, five children, youngest six years. Admitted on surgical service March 11, 1933. Patient stated that for the week prior to onset of present illness she had had a "cold." March 10 had a severe chill followed by low abdominal pain more pronounced on left side. Pain also extended to right shoulder. Vomited five times; no diarrhea. On day of admission temperature 103.5° F., pulse 100, leucocytes 24,400, polys 97 per cent. Examination on admission: lungs clear, fauces reddened, abdomen distended. Lower abdomen was painful to pressure with rebound tenderness on left side. Cervix normal position; external os admitted index finger, lateral fornices nothing remarkable; posterior fornix indefinite tender fullness. Cervical smear showed pus cells with variety of organisms (types not specified). The above examination was made and recorded by the same interne who had been on the gynecologic service three months before, when the first case here reported was admitted and studied. This fact makes of interest his recorded impression note: "Pelvic inflammation, acute, and in view of onset following an upper respiratory infection believe that the pelvic infection might well be of the pneumococcus type. Gonococcus to be ruled out."

March 15: Patient had pain in right chest, pleuritic in character and on auscultation an occasional friction rub was heard with somewhat diminished breathing; respirations 22. Temperature ranged lower, fluctuating to 100.5° F., pulse 90. Abdominal symptoms somewhat improved. Patient continued with irregular temperature, highest 100° F. with pulse 80-90 until March 30, 19 days after admission. She was then transferred to gynecologic service as the pelvic mass had developed, pushing the cervix high and somewhat to the left. The fluctuating mass behind the cervix could be felt above the symphysis. Patient taken to operating room at once for a posterior colpotomy. While on the operating table before the colpotomy was done, a sound was introduced into the uterus and a moderate quantity of pus escaped; this was collected on a swab. On opening the culdesac a large amount of thick flocculent, odorless pus was evacuated. A sample of pus from the abscess and the swab from the uterus were sent to the laboratory. From the pus obtained from the uterus a smear showed gram-positive bacilli with the same organism in culture. No streptococci seen. The pus from the abscess yielded gram-positive cocci in pairs producing green color in broth and without hemolysis on blood. Bile solubility definitely positive. Pneumococcus Type IV.

CASE 3.—This case is of especial interest and a search of the literature fails to discover a similar one.

Mrs. J. S., aged thirty-six, the wife of a physician, was first seen by me in January, 1924. At that time she had two children, aged seven years, and eleven months. She had been ill since the birth of the last child. This last labor, occurring Feb. 9, 1923, was normal in every respect. Postpartum temperature was normal for three days, then she felt chilly on several occasions, with temperature of 101° F., pulse 90. Lochia not remarkable. During the night of February 13 she had repeated slight chills and aching of the muscles; the following day temperature was 102° F., pulse 100. That night she complained of nausea and severe abdominal "cramps." The following day she was somewhat more comfortable, with lower temperature, and on eighth day it became normal and remained so until the eleventh day when she went home. Her urine having contained much pus, her symptoms were assumed to be due to pyelitis. Following her return home she developed arthritis,

and a number of abscessed teeth were extracted, with some temporary relief. She had much backache and frequent temperature of 105° to 106° F. Some urinary frequency. On Aug. 23, 1923, she was admitted to the hospital for urologic study. Catheterization of the ureters showed normal discharge of urine, and no pus was found in collected samples from either side. There was pain in lower right quadrant during the six days in the hospital; temperature fluctuated irregularly to 101° F. Pelvic examination at this time was said to be negative.

Her subsequent progress was not satisfactory. Her joint pains persisted and on several occasions she was confined to bed with temperature and pain in lower abdomen. The latter part of January, 1924, eleven months after confinement, pelvic examination by me revealed a tender mass the size of a small grapefruit on the right side; uterus somewhat anterior and pushed to the left. Left adnexa free. A diagnosis of right ovarian abscess at that time was made. As the patient's general condition was not good it was decided to drain the abscess through the vagina and allow her condition to improve before removing the sac. Feb. 7, 1924, a posterior culdesac opening was made but no pus found. The mass was firm and very fixed. Leucocyte count was 10,500, 81 per cent polynuclears. For the following ten days temperature was of septic type; pulse 90-100. On February 26, ten days after the colpotomy, a laparotomy was done. Through a transverse incision a mass the size of a small grapefruit presented on the right side. A small area of the upper portion was free of adhesions but at all other parts it was firmly adherent to intestines and pelvis. The appendix and cecum were involved in the mass. The adhesions to the pelvis were extremely dense. The broad ligament was markedly thickened. The bowel was carefully freed by sharp dissection. The attachments of the mass posteriorly were very thick and in freeing it here a small amount of thick odorless pus escaped. The mass could then be removed. A rubber pelvic drain was placed through the right angle of the incision. The left tube and ovary were normal and free of adhesions. Her convalescence was uneventful and she was discharged on the twenty-third post-operative day and since the operation she has been in the best of health.

The gross pathology here did not conform to the ordinary pelvic infection. The mass consisted of ovary and tube, the ovary composing the greater part of the mass. The pathologist reported numerous abscesses of various sizes throughout the ovarian mass. The tube was much thickened and contained a small amount of pus similar to that in the abscesses of the ovary. Smears from these abscesses showed gram-positive diplococci. Cultures from the various abscesses yielded the same organism in pure culture, all of which answered to the requirements of the pneumococcus. Diagnosis: right salpingitis and multiple ovarian abscesses of pneumococcus origin.

It is somewhat difficult in this case to reconstruct the course of events leading to the final pathology. The onset three days post-partum was suggestive of a pneumococcus pelvic infection. The initial chill followed by a rise in temperature and symptoms of general systemic infection, which in turn were followed two days later by further chills with severe "crampy" pains in lower abdomen, was in every way characteristic. The fact that these symptoms subsided in a few days may be accounted for by a pneumococcus of low virulence becoming confined to the tube, with later involvement of the ovary. The attacks of pain and temperature on several occasions during the succeeding months may have indicated a new abscess in the ovarian mass until finally the pathology found at operation had developed.

Certainly urologic examination during the time when these attacks were occurring, yielded no evidence to justify regarding such attacks as due to a pyelitis. Finally, removal of the mass resulted in prompt and complete recovery.

The literature yields cases comparable to these here reported. Wolfsohn reports a case of a thirty-seven-year-old woman, ill fourteen days; large collection of pus below the umbilicus evacuated. Postoperative pneumonia; recovery. Also a woman of twenty-eight years who on the day following an abortion was taken suddenly ill with abdominal pain and a rise in temperature. A large culdesac collection was later evacuated with prompt recovery. Pneumococcus found. Gibson reports a case of an unmarried woman twenty-five years old who had been ill for three weeks with "cold" and mild abdominal symptoms. Acute onset with chilly feelings, cramps, diarrhea, and vomiting. Median laparotomy yielded the characteristic pus confined to the lower abdomen. Culture of pus from the nose and throat showed pneumococcus Type I. Cultures from vagina and cervix were negative. In a discussion of Gibson's paper, C. H. Peck, New York, reported the case of a woman thirty-two years old who had been operated upon for mastoiditis. Five days later a large right-sided abdominal abscess developed and was opened. Pneumococcus, Type III, was found in the pus of the abscess and in the mastoid. Death followed.

A review of the reported cases also suggests that the pneumococcus may be the sole causative agent in infections following abortion or labor, occurring either as a very early acute puerperal process or as one appearing several weeks postpartum. One patient in Wolfsohn's series developed an infection twenty-four hours after an abortion. Baetjer³ reports a woman twenty-seven years old who five weeks after normal labor and uncomplicated puerperium, was suddenly seized with acute pelvic pain with the rapid development of a generalized pneumococcus peritonitis which resulted in death. At autopsy the left tube was apparently the focus.

The second case of Baetjer's was a woman aged twenty-five, who six weeks after a normal labor and puerperium, was seized suddenly by severe pain in the lower abdomen. There had been no preceding indications of upper respiratory infection. Blood culture was negative. Laparotomy evacuated a thin, turbid, purulent fluid. Culture was a pure growth of the pneumococcus, Type II. Two days later pleurisy and a lobar pneumonia developed, followed by an abscess of an upper lobe which finally ruptured, and recovery resulted. At the time of the pneumonia, the blood culture was positive. Baetjer records a low leucocyte count in his two cases.

Two cases reported by McCord⁴ occurring in the early puerperium are of interest. The first patient was a negress, eighteen years of age. On the third day following a spontaneous labor she was seized with a severe pain in the lower abdomen. She had a slight chill and a rise of temperature to 103.2° F. with a pulse of 128. This case progressed rapidly to the picture of general peritonitis. The abdomen was opened under novocaine and a large amount of pus was drained. The patient died four days after onset of illness. The blood culture and smears both at operation and autopsy were positive for the pneumococcus.

His second case was also a negress, aged eighteen, admitted in labor. She was delivered spontaneously and returned to the ward with normal temperature, pulse, and respiration. Twelve hours later she complained of being cold and of pain in the abdomen. Her temperature was 103.2° F., pulse 108. She died four days later. Autopsy showed a general peritonitis and endometritis with involvement of tubes and ovaries. The blood culture was reported as pneumococci. In neither of McCord's cases had a vaginal examination been made.

A somewhat similar case is reported by Seymour.⁵ A woman of twenty-four was delivered by low forceps. Seven days postpartum, she had a chill and temperature

rise to 103° F. The following day the uterus was swabbed out and smears showed a gram-positive diplococcus. Peritonitis developed rapidly. Abdomen was opened with the evacuation of two pints of turbid fluid. Drainage of the pelvis and abdomen resulted in eventual recovery. The pus yielded a pure growth of pneumococcus.

The French literature yields two cases. The first is that of Apert.⁶ A young primipara with a marked coryza and a profuse serious nasal discharge, was delivered normally of twins. The day following delivery there was a sudden rise of temperature and abdominal distention. The following day there was profuse diarrhea with continued fever. Fluid was diagnosed "at the base of peritoneal cavity." (In culdesac?) A small low median incision was made and a serofibrinous, somewhat purulent, fluid escaped. Examination showed it to be pure pneumococcus. A suppurative otitis developed and pus from both nose and ear also showed the pneumococcus.

Darrè⁷ and two collaborators report a woman twenty-six years old who had had a normal confinement. Three weeks postpartum she was confined to bed for a few days with a pain in the right iliac fossa accompanied by some diarrhea and a yellowish leucorrhea. She had apparently been well but five days later a similar attack occurred. Two months postpartum she was seized one morning with acute abdominal pain, vomiting, and profuse diarrhea. She was admitted to the hospital on the same day. Twenty-four hours later she had violent abdominal "cramps." Examination showed pouch of Douglas painful but no masses were recognized. Low median laparotomy was done with evacuation of yellowish, odorless, fibrinous pus from the pelvis. Pelvic drainage; final recovery. Pus showed pneumococcus.

A review of these and other cases makes it reasonable to divide pneumococcus pelvic infections in adult females into four groups:

I. The pelvic abscess in which the infection, having become walled off early, remains confined to the pelvis.

II. The generalized peritonitis in which the entire abdominal peritoneum becomes the abscess sac.

III. An infection confined to the tube and ovary. (Third case reported by writer.)

IV. Puerperal infection following either abortion or labor at term. Such infections may occur early in the puerperium, or during the later weeks of involution. Obviously such an infection at that time may develop into a condition to be classified under one or another of the above groups.

The recognition of these four groups has a practical bearing on the diagnosis, prognosis, and treatment.

Those who have written on the subject have discussed the etiology thoroughly. The review of reported cases indicates that on clinical evidence the majority have their origin in the genital tract. The fact, however, that pneumococcus peritonitis may occur in males, both children and adults, as proved by reports of a number of observers, points to other possible avenues of invasion. The blood stream, lymphatics, and intestinal tract have been discussed. If the infection in males finds its way to the peritoneum by one of these latter channels, it is logical to assume that at least a small proportion of cases in females may also occur in the same way. We are justified in assuming,

however, that a very large proportion of these infections in females do reach the peritoneum by the genital tract.

Michant⁸ in 1901 suggested classifying cases of pneumococcus peritonitis into primary and secondary, and this classification generally has been followed. I believe, with some others, that this classification should, for a better understanding of the condition, in adults at least, be abandoned. Pneumococcus peritonitis is a comparatively rare complication of pneumonia and in some reported cases pneumonia has followed, instead of preceded, the invasion of the peritoneum. To adhere to this classification ignores the less obvious focal points from which an infection may spread. A number of cases reported in adults do give a definite history of an upper respiratory infection which antedated or was coincident with the pelvic infection. My first patient was ill several days with what was considered the "flu." The second had a definite upper respiratory infection.

If in the future more careful inquiry is made, I believe that a considerable number of these cases will reveal evidence of such infections. Granting the possibility that these conditions do play a rôle in the pelvic infection, there arise some pertinent questions. Are the latent pneumococci harbored in the nose and throat of many normal persons, activated by the bacteria of the "common cold," making it possible for them to invade the blood stream? Or are these foci the source of an infection that is carried directly to the genital tract? McCartney⁹ has argued convincingly for direct invasion of the genital tract in children. He produced the disease in a monkey by that means. It is much easier to accept this view in the case of children than it is in adults. If, however, these pneumococcus vaginal infections in children invade the uterus and pelvis so readily, these bacteria possess a tendency to spread on their mucous surfaces that the gonococcus does not, as gonorrheal pelvic infection in children is extremely rare.

If it be a blood stream infection, it must be assumed that it reaches the uterus or tubes and produces an endometritis or salpingitis in much the same way as the tubercle bacillus, for all other infections of the pelvis are due to direct invasion of the canal. Unfortunately for the blood stream theory, animal experimentation has added nothing to its support, and clinically, a positive blood culture is not always found. So far as adults are concerned it must be admitted that there is at present no evidence that satisfactorily accounts for all cases of pneumococcus pelvic infections.

The clinical manifestations of the disease in adult females are quite constant and characteristic. The outstanding features are:

1. There is often a previous indisposition usually associated with the symptoms of an upper respiratory infection. When a pneumococcus pelvic infection is suspected, careful inquiry on this point should *always* be made.

2. The invasion of the peritoneum is characterized by its sudden onset. There are chills or "chilly feelings." The pain is sudden, severe, and located in lower abdomen. The patient often describes it as "crampy" in character. This may be accounted for by the fibrinous exudate that the pneumococcus so promptly calls forth and the effect of peristalsis upon these surfaces. Further distribution of the pain will depend upon the spread of the process. Nausea or vomiting is present in a large proportion of cases, either at the onset or later. In contradistinction to peritonitis from other causes, diarrhea is not uncommon. The temperature may rise to 103° or more following the chill. The pulse rate at first is high, but with early localization, the rate drops out of ratio with the temperature, which may remain high. A high leucocyte count early of 20,000 or more is usual with a polynuclear count of 90 per cent or higher.

Invasion of the blood stream may or may not take place. Blood cultures, if positive, may be found early or at any stage of the disease. The presence of the pneumococcus in the vaginal discharge is like the positive blood culture, an uncertain quantity. Positive vaginal smears have been recorded in about 50 per cent of cases in children. Adult cases have not been carefully enough studied to make observations on this point of value.

It is not to be expected that the physical signs associated with a pneumococcus pelvic infection in adults will differ essentially from similar pelvic infections from other causes. Of much importance is the early tenderness, and the sensation of fullness in the culdesac imparted to the examining finger. The pneumococcus on a serous surface promptly calls forth a fibrinous exudate and in addition it is a rapid pus producer. This may account for these early pelvic findings. With localization, the culdesac collection will usually develop very rapidly or, less commonly, it may require a number of days before the abscess markedly displaces the cervix.

With a fulminating spread the evidences of general peritonitis are, of course, present. The one distinguishing point, however, is the rapid formation of pus which takes place earlier and in far greater quantity than in peritonitis from appendicitis or other causes. It should be possible to determine early the presence of this fluid. Some observers have noted that the abdominal wall is less tense than in other forms of peritonitis and that later it may even have a somewhat doughy feel. The amount and character of pus may account for this.

It is not surprising that a preoperative diagnosis has very rarely been made. The second case here reported was diagnosed by the interne upon the history, the physical findings and the fact that he had become pneumococcus conscious. The first essential for the diagnosis of any pathologic condition is that the clinician shall have in mind the possibility of its occurrence. These patients have been mis-

taken and operated upon for various abdominal conditions, or the abdomen has been simply drained on general surgical principles. In practically all of the reported cases the diagnosis has only been made postoperatively by the bacteriologic findings. The surgeon, however, who has seen the characteristic odorless, flocculent pus of these cases, should, in the majority of instances, be able to make a table diagnosis. This in itself is important as it forestalls a futile search for an abdominal focus and enables the surgeon to confine his attention to establishing adequate drainage. Undoubtedly, with the condition in mind and with due regard to the history and clinical features, these cases in the future will be more frequently diagnosed.

As to prognosis, in reviewing the adult cases, two facts stand out prominently. Patients belonging to Group I recover promptly on draining the abscess by posterior colpotomy. Low abdominal drainage of this group, as was done in some cases, seems not to be followed by equally good results. In contrast to these results in Group I, the cases of generalized peritoneal infection of Group II have a high mortality. This is especially true of those cases that occur early postpartum. Other factors such as the virulence of the organism, and complications, play the same rôle in the prognosis as in all other infections.

It would seem somewhat premature at this time to discuss at length the treatment of these patients. The treatment of the patients in Group I is simple and satisfactory. The treatment of the patients in Group II by drainage has not been promising. It would appear at present that until the clinical and laboratory features have been more carefully elaborated with a view to determine better the criteria upon which an early diagnosis may be made, there is little hope of improvement in the present mortality of this group. If there comes a time when it is possible, on the evidence, to drain the culdesac early, it is not unreasonable to expect that such prompt drainage would result in the infection remaining localized in the pelvis and that in fewer cases would it spread to the general peritoneum. Colpotomy is such a simple and safe operative procedure that there is little that can be urged against it.

In the presence of a well-developed general peritonitis adequate drainage is the only hope. In such a case it would seem that a median pelvic drain with bilateral flank drainage would meet the indications best.

CONCLUSIONS

1. Pneumococcus peritoneal infections in the adult female are of more frequent occurrence than published reports would indicate.
2. They have an especial interest for the gynecologist and obstetrician.

3. The genital tract is the most frequent path of infection, but a small percentage probably occurs by other means.

4. More careful histologic and bacteriologic autopsy studies of the pelvic organs should be made when opportunity presents.

5. The disease in adults should, because of the clinical features peculiar to them, be studied apart from the disease as seen in children.

REFERENCES

- (1) *Gibson, C. L.*: Trans. Am. Surg. Assn., Philadelphia, 1925. (2) *Wolfsohn, G.*: Zentralbl. f. Chir. 57: 1930. (3) *Baetjer, W. A.*: Trans. Assn. Am. Phys., Philadelphia, 1925. (4) *McCord, J. E.*: AM. J. OBST. & GYNEC. 16: 2, 1928. (5) *Seymour, H. F.*: Brit. M. J., May 26, 1928. (6) *Apert, M. E.*: Bull. et mém. de la Soc. Med. des Hopitaux de Paris 36: 1877, 1930. (7) *Darré, H. L., and Laederich, H. Hamou*: Bull. et mém. de la Soc. Med. des Hopitaux de Paris 33: 1738, 1930. (8) *Michant*: Thèse de Paris, 1901. (9) *McCartney, J. E.*: J. Path. & Bact. 26: 507, 1923.

1255 DELAWARE AVENUE

INTRAUTERINE APPLICATION OF CARBON IN INCOMPLETE ABORTION*

B. H. CARROLL, M.D., TOLEDO, OHIO

AT PRESENT the accepted treatment of abortion is along the well-established conservative lines. Instrumentation in which the uterine cavity is entered, cervical or vaginal packs, even examination except under sterile conditions, are, generally speaking, contraindicated. However, it may be necessary to remove the uterine contents. In the presence of infection this operative procedure carries a very definite risk to the mother. The cause of death in nearly every case is directly or indirectly due to infection. Attempts to safeguard this procedure by the use of local antiseptics have not been successful. The uterine cavity cannot be made sterile except for very short periods of time.

During the war, German research workers revealed that carbon produced at a low temperature had a much greater power of adsorption than the average carbon made without careful thermal control. This carbon is known as activated carbon and has from thirty to three hundred times the power of adsorption possessed by ordinary carbon. The highest grade is 99.9 per cent pure. Consequently it is very porous and easily pulverized into the finest powder. A comparatively

*Read at the Forty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., September 6, 7, and 8, 1934.

small amount of carbon, when powdered, offers a large surface for chemical action.

Adsorption may be defined as the process whereby a substance becomes a part of another and remains in a state midway between a mechanical mixture and a chemical combination. Koenig states that the power of adsorption depends upon (1) the extent of surface energy; i.e., the size of the free surface, (2) the surface tension between adsorbent (carbon) and the liquid; and (3) the surface activity of the liquid.

The use of carbon to absorb and adsorb gases and toxins from the intestinal tract and from suppurating wounds is well known.

The veterinarians, appreciating the dangers of decomposing and infected material left in the uterine cavity, to be sloughed and expelled by nature, were the first to try to ameliorate the symptoms and hasten the process of healing by using this activated carbon. They observed no unfavorable symptoms or reactions. The symptoms of toxemia promptly subsided. Fewer cases of general sepsis developed in the animals so treated, and there was a disappearance of the offensive odors so characteristic in these cases.

Shortly after the reports of the veterinarians, activated carbon was used for similar conditions in women. From 1925 to 1932 there appeared in the foreign literature, mostly German, reports from fourteen physicians. These articles included some laboratory reports but were mostly their clinical experiences.

The general procedure was as follows: In a case in which it was reasonably sure that the infection, if present, had not extended into the blood stream or parametrial tissues, the patient was prepared in the conventional way, and the cervix exposed and dilated, if necessary, to admit the carbon. Any tissue in the cervix was removed. Some preferred to empty the uterus before inserting carbon. The uterine cavity was then filled with carbon. Merck & Co., Darmstadt, supplied carbon in the form of sticks or pencils, about 1 cm. thick and 5 cm. long. Two or three sticks of carbon were carefully placed in the uterine cavity, sometimes followed by a light cervical gauze pack. A black foaming mass of material would exude from the cervix including at times small pieces of carbon. The patient was returned to bed under general care, and ergot, quinine and pituitrin were given as a routine treatment. The lochia was black, due to the carbon, for several days. Convalescence was usually prompt.

The number of cases reported was well over three hundred. All reports were in accord, that no injury was done to the tissues as a result of the intimate contact with the carbon. They were all agreed that toxic symptoms were promptly abated and the general condition of the patient improved. In their records there were no cases of general sepsis attributed to the use of carbon and fewer cases in which there was extension of the infection into surrounding tissues. There was a shorter convalescence. If the uterus did not expel its contents in a few days either more carbon was inserted or the products of conception removed and carbon replaced. Some authors spoke of this first use of carbon as a prophylactic treatment.

The advantages of this method of treatment over other methods were given as follows: The action of carbon is entirely local. It is not injurious to healthy tissue. This activated carbon is rapidly and easily pulverized, completely covering the uterine wall and filling all small cavities and irregularities. By its tremendous power of adsorption, bacterial toxins in the uterine cavity are adsorbed. Resorption by the patient of this combined toxin is impeded if not actually prevented.

Carbon is also known to have powerful absorbing qualities, thus taking up the secretion from the endometrium. By absorbing this secretion the nutrient medium

is definitely changed and this may influence the life and virulency of the organisms. Also the marked absorptive power of carbon causes a local hyperemia and increases the patient's resistance to infection. Some authors feel that there is a direct mechanical stimulation of the reticuloendothelial system to a phagocytosis by the carbon. It has been shown that carbon changes the pH concentration of a medium to the acid side, and this has a pernicious influence on streptococci. Acting as a foreign body in the uterine cavity, it stimulates contraction of the muscle. Small particles of carbon dust promote rapid thrombus formation in the mouth of vessels.

Clinical results reported included a sudden fall of temperature in febrile cases with no recurrence of fever; the afebrile patient remained afebrile; there was immediate cessation of hemorrhage; lochia containing carbon lasted from three to five days. There was a marked improvement in the general condition of the patient, and prompt deodorization. The hospital days were reduced from twelve to ten, and fewer complications and no injurious effects were noted.

In our early experience in using carbon the results were not as encouraging as we had hoped for, although the patients were less toxic and temperatures lower; the fever persisted in some patients and several had hemorrhage.

These patients were in the third and fourth month of their pregnancy, at which time the placenta has developed to a considerable size and has characteristic qualities. We know that bacterial growth is most prolific on devitalized tissue and that the hemorrhage usually comes from the placental site. It seemed plausible to us that by removing the placenta and products of conception first, then the action of the carbon would not be handicapped or overwhelmed by a mass of decomposing tissue. Proceeding on this theory, our patients were first given a physical examination and a definite diagnosis of incomplete abortion or abortion in progress was made. We tried to diagnose other pelvic pathology, especially extension of infection beyond the uterine cavity. If our findings were negative we proceeded along the usual lines to empty the uterus. It was necessary to dilate the cervix in about half of the cases, placental or ring forceps being used to grasp the retained tissues. Occasionally it was necessary to use a dull curette. Care was used to traumatize the normal tissue as little as possible, in the operation. After emptying the uterus the cavity was carefully filled with carbon pencils.* Almost immediately a frothy black mixture exuded from the cervical os, which is the lochia of the succeeding few days. Five of our patients continued to have hemorrhage so that it was necessary to put in a light gauze pack.

The patient was then returned to bed and given general nursing care. We felt that with a clean uterus and the carbon acting as a foreign body to stimulate contraction, no specific medication was indicated. Consequently, we deviated from the German procedure and did not use ergot, pituitrin, or any of their derivatives. A few patients were given transfusions.

Following this type of treatment, we have the records of 106 consecutive cases of abortion in which carbon has been used in the uterine cavity. The length of time the abortion had been in progress varied from two months down to the therapeutic abortion. On the day preceding or the day of the operation sixty-eight patients carried a temperature of 100.2° or above. Thirty-eight patients had a temperature

*Imported by Merck & Co., Rahway, New Jersey.

of less than 100.2° and are considered, for this report, as afebrile. As might be expected, a large percentage of the whole group had a primary or a secondary anemia. Half of the patients had a hemoglobin of 60 per cent or less, one-third were below 50 per cent, 7 patients were below 30 per cent.

With each patient the uterus was emptied and carbon inserted as promptly as possible after the diagnosis was made, usually within twenty-four to forty-eight hours.

In this group there were no deaths. Ten patients of this series remained in the hospital more than seven days. Two were held for further transfusions and general building up. Eight patients continued to run a temperature over a period of several days. One of these had a severe pyelitis on admission, which was probably the exciting cause of the abortion. A second patient with active tuberculosis had a therapeutic abortion in which carbon was inserted; two months later a dilatation and curettage was done because of uterine bleeding. A piece of placenta was recovered and carbon was inserted. This patient promptly developed a parametritis. A third patient had a well-established parametritis on admission to the hospital and was about bled out. After removing tissue which was protruding from the cervix, carbon was inserted to control the hemorrhage. This patient had a stormy convalescence, forty-six days in the hospital. Five other patients developed a parametritis after using the carbon. Whether this complication was due to the already infected abortion or occurred in spite of our procedure, I am not prepared to say. This is a morbidity rate of 8.8 per cent for the infected cases and 5.6 per cent morbidity rate for the whole group.

The average time of all patients in the hospital was seven days after operation, a saving of 25 per cent in hospital days when compared with conservative treatment. After dismissal from the hospital no unfavorable symptoms were reported. Occasionally small flecks of carbon would be recovered from the vagina two weeks after operation, but this caused no distress. The menstrual cycle was reestablished as usual. Seven of these patients have since become pregnant. Three were delivered of normal babies, two induced abortion upon themselves and are included in the series a second time. The terminations of the other two are unknown.

For obvious reasons, it is difficult to check by laboratory tests the contention of the foreign workers, as enumerated earlier in this paper.

Carbon changes the pH concentration of a culture medium toward the acid as is shown in Table I. This increased acidity affects the rapidity of growth and staining characteristics of the streptococci.

TABLE I

Br. Br. Culture		Before incubation	pH 8.0
Br. Br. Culture		24 hr. incubation	pH 7.4
Br. Br. Culture	plus carbon	24 hr. incubation	pH 6.8
Br. Br. Culture (pH 0.8) plus Strep.		24 hr. incubation	pH 6.6
Br. Br. Culture (pH 0.8) plus Strep.	plus carbon	24 hr. incubation	pH 6.2
Br. Br. Culture (pH 0.8) plus Strep.		48 hr. incubation	pH 6.4
Br. Br. Culture (pH 0.8) plus Strep.	plus carbon	48 hr. incubation	pH 6.0
Br. Br. Culture (pH 0.8) plus Staph.		24 hr. incubation	pH 6.4
Br. Br. Culture (pH 0.8) plus Staph.	plus carbon	24 hr. incubation	pH 6.0

Gram stain smear from Br. Br. culture plus streptococcus plus carbon after twenty-four hours' incubation show a few organisms, which take a negative stain.

Subculture made on fresh Br. Br. culture shows a growth of streptococcus at the end of twenty-four hours.

Gram stain smear from Br. Br. culture plus staphylococcus plus carbon twenty-four hours' incubation, no organisms found.

Subculture made on agar slant shows slight growth of staphylococcus.

This increase of acidity may well take place in the uterine cavity inhibiting or interfering with bacterial growth.

There were no postoperative hemorrhages in those cases in which all of the material was removed. Carbon acting as a foreign body, probably, helps to keep the uterus contracted and also hastens coagulation.

CONCLUSIONS

This is a relatively small number of cases from which to draw anything but general conclusions. It does seem that the patients are not endangered by the carbon per se; that symptoms of toxemia were promptly relieved. There was a 25 per cent shorter convalescence. There were only six patients in whom the infection extended into the parametrial tissues after the use of carbon. There were no deaths.

These results, which are in close accord with those already published, should warrant further investigation as to the advisability of treating incomplete abortions, whether infected or not, with activated carbon.

REFERENCES

- (1) *Wetherspoon, J. T.*: AM. J. OBST. & GYNEC. 26: 367, 1933. (2) *Curtis*: Obstetrics and Gynecology, p. 1102. (3) *Luaces, E. L.*: Toledo, Ohio, Personal communication. (4) *Koenig*: Pharm. Ztg., No. 101, 1928. (5) *Geller, F. C.*: Zentralbl. f. Gynäk. 53: 82, 1929. (6) *Wedekind, T.*: Deutsches Arch. f. klin. Med. 163, 164, 202-219, 1929. (7) *Louros, N., and Scheyer, H. E.*: Ztschr. f. d. ges. exper. Med. 55: 724, 1927. (8) *Nahmmacher, H.*: Surg. Gynec. Obst., May, 1930. (9) *Beuthner, B.*: Arch. f. Gynäk. 141: 125, 1930. (10) *Benthin, W.*: Zentralbl. f. Gynäk. 52: 858, 1928. (11) *Gickler, H.*: Beitr. zur klin. d. Tuberk. 72: 32, 1929. (12) *Graf, H.*: Deutsche Tierarztl. Wehnschr. 36: 807, 1928. (13) *Geller, Fr. Chr.*: Fortschr. d. Therapie, Leipz. 7: 714, 1931. (14) *Jetto, Rocco*: Rassegna d'ost. e ginec. 41: 720, 1932. (15) *Merek & Co., Inc.*, Rahway, N. J.: Personal communication.

Wallis, Otto: A Case of Disgerminoma Ovarii, Zentralbl. f. Gynäk. 57: 729, 1933.

A seventeen-year-old girl entered the obstetric service under the impression she was pregnant and was subsequently found to have a large solid ovarian tumor weighing 5,300 grams. The tumor fell into the group designated by Robert Meyer as disgerminoma. The right ovary appeared to be normal and was not removed. There had been no disturbance of menstrual or sex functions, but there was a mild grade of malnutrition, infantilism and hypogenitalismus.

Disgerminomas are tumors arising from an undifferentiated germinal epithelium of the gonad, and do not possess any hormonal function. They have previously been described as large cell alveolar sarcoma, endothelioma, lymphangioendothelioma, granulosa cell tumor and chorioectodermal epithelioma.

WILLIAM F. MENGERT.

MONOAMNIOTIC TWIN PREGNANCY*

A CASE RECORD WITH REVIEW OF THE LITERATURE

JAMES K. QUIGLEY, M.D., F.A.C.S., ROCHESTER, N. Y.

INCIDENCE.—The rarity of monoamniotic twin pregnancy is sufficient reason for this case report. J. W. Williams¹¹⁰ in a brief reference to this condition said that there were 44 cases in the literature, those of Holzapfel's series. DeLee in the 1928 edition of his Textbook said 40 cases had up to that time been reported. However, one year prior to Holzapfel's⁵¹ monograph or in 1903, Alfieri⁵ had collected and described in detail 71 cases. These monographs together with that of Ahlfeld⁴ remain the best contributions to the study of this interesting and unusual condition.

There are but eight references with case reports in the American literature, from that of Reynolds⁸⁷ in 1835 to T. J. Williams in 1931—only one case in the last twelve years. In none of these articles is there a thorough review of the literature and the case here reported is the only full-term pregnancy and the only instance of a surviving child in the American literature.

Resinelli⁸⁸ estimates that monoamniotic twin pregnancy represents 2.11 per 100 cases of uniovular twins. Alfieri found six monoamniotic out of 1,535 twin pregnancies; Ahlfeld in 506 twin pregnancies found 60 monochorionic and three monoamniotic. It would seem that Müller's estimate of one per 6,000 births is too great an incidence, for this would mean one monoamniotic for every 70 cases of twins and the paucity of cases in the literature does not warrant such an estimate. Contrasted with Müller's⁷² estimate of one per 6,000 is that of Rosenberg of one to 60,000 births.

Dietrich²⁷ said, "It is given no obstetrician to see more than one case in his experience." That is not quite true, for Schultz,⁹⁷ Spaeth,¹⁰⁵ Th. Wenzel,¹¹⁶ Wolf,¹²² and Pallin⁸⁰ have published descriptions of two cases each. Every author writing upon the subject of monoamniotic twin pregnancy has emphasized its extreme rarity.

Jeannin⁵⁴ says that in a triple pregnancy two of the fetuses may be contained in one amnion. I found eight such cases reported. Ausch⁶ and Hauser⁴³ have seen in two cases of quadruple pregnancy, three of the fetuses enveloped by one amnion and lastly, Caseaux cites a case of monoamniotic quintuple pregnancy delivered in Pignè.

In the recent well-known case of Dr. DaFoe²⁵ in Canada of quintuplets there was one placenta and five amniotic sacs.

*Read at the Forty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., September 6, 7, and 8, 1934.

NOTE: For lack of space the tabulation of cases could not be included here, but may be found in the current Volume of the Association's Transactions.

CASE REPORT

Mrs. C. O'K., para i, aged thirty-four, married three and one-half years; last menstrual period, Jan. 29, 1933, quickening June 12. Expected date of delivery, Nov. 5, 1933. Twins were diagnosed September 29 and aside from discomfort from tremendous distention (height of fundus on November 9 was 45 cm.), the course of her pregnancy was uneventful. Only one fetal heart was heard at her numerous prenatal visits and that was in the right flank. One vertex descended into the pelvis a month before delivery. Because of extreme discomfort and the fact that the patient was a few days past her estimated date, labor was induced by castor-oil and quinine on November 10.

The labor was short for a primipara, eight hours and thirty-seven minutes. The amniotic fluid was meconium colored on rupture of the membranes and naturally it was thought that the first child might be in danger. This child was delivered

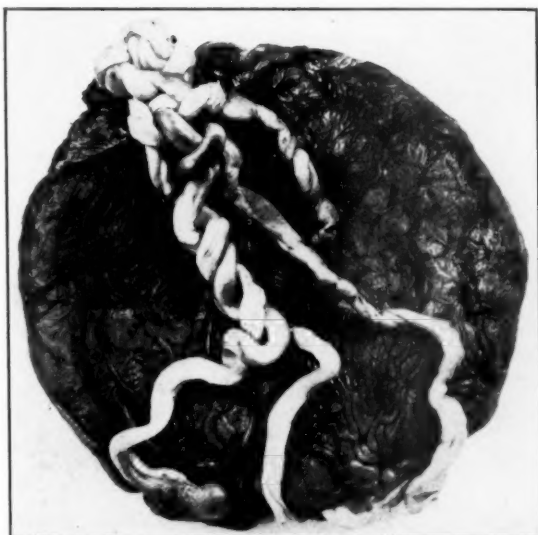


Fig. 1.—Fetal surface of the placenta showing knot formation and twisting of the cords and their marginal insertion.

L.O.A. spontaneously and was in good condition. The second child in R.O.P. position was delivered by an easy Scanzoni maneuver. It was born in pallid asphyxia, the heart action was feeble and 40 to the minute. All known methods of resuscitation were employed, such as tracheal catheter, the administration of $\text{CO}_2\text{-O}_2$ mixture, Alpha lobelin injection and adrenalin injected into the heart which continued to beat for twenty-five minutes, but respiration was never established. The twins were females and weighed, first twin (survived) 2,975 gm., second twin 3,114 gm.

The cause of the asphyxia was discovered on the delivery of the placenta which measured 29×23 cm. and weighed 1,545 gm. There was only one amniotic sac, the cords were inserted marginally, 9 cm. apart; the insertion was almost velamentous; there was no anastomosis. There was no indication of a partition remnant. The cord of the second baby was entwined with that of the first and tied into an indescribable mass of knots, almost the size of a man's fist. The cord of the first baby passed through this mass but was not involved in it.

HISTORY

Hippocrates mentioned monochorionic twins but said nothing as to both being enclosed in one amnion. Mariceau, Levret and Bandelocque denied its existence. Jeannin⁵⁴ and Eleuterescu³² of France both credit Viardel, a fellow countryman, with the first description of this condition in 1671, Alfieri, however, contradicts this and says that in 1612 Boccacini and in 1,649 Jakob von Back⁷ demonstrated that twins might both lie in the same amnion. Thus three or four descriptions appeared in the seventeenth century, only one in the eighteenth and beginning with Tiedeman's¹¹⁰ case in 1805, there were up to 1903, 71 cases collected by Alfieri. In 1904, Holzapfel collected 39 already reported by Alfieri and three, including his own, not in Alfieri's collection. I found eight cases reported prior to the monographs of Alfieri and Holzapfel but not included by either and I have collected 30 additional cases reported since 1904. These together with the one here reported totals 113 cases. However, included in Alfieri's series were four credited to Weiss, cited by



Fig. 2.—Maternal surface of the placenta.

Hink.⁴⁰ Both Alfieri and Hink doubt, because of the rarity of the condition, that one man had observed as many cases. Allowing for this discrepancy then, it might be said that to date, 109 cases have appeared in the literature.

ETIOLOGY

There are two theories as to the origin of monoamniotic twin pregnancy. The first, or primitive duality, in which there are originally two amnions, the partition between the two sacs is broken down early in fetal life; the second, that of primitive unity, in which case there is one amnion from the beginning. Two blastodermic vesicles meet and join and are enveloped by one amnion.

There are many supporters for both theories. Kleinwachter,⁶⁰ Leishman and Ahlfeld believe in the first, that there are originally two amnions and that the partition between disappears. How this comes about is a matter of conjecture. Kleinwachter holds that due to movements of the fetuses, a tear occurs and the remainder atrophies. Ahlfeld thinks the pulsation of the two close lying cords causes a lacera-

tion through friction. Holzapfel agrees with this. In favor of primitive duality is the presence of a reste or remnant of the partition, between the cord insertions on the placenta. Ahlfeld, Holzapfel and Podzahrodsky⁸⁶ have minutely described such remnants and a number of other observers mention their presence, while in more than a dozen cases it was distinctly stated there was no partition reste found.

Schultze and Bumm⁹ are proponents of the primitive unity theory. They argue that if we are to believe in the tearing of a partition between two separate amnions, it would occur in biovular pregnancies as well. Some of the cases have shown a common cord for both fetuses, blended or anastomosed; this, of course, is in favor of the primitive unity idea.

Bifurcated cords were present in five of this series and in many, the cord insertions were very close together, this arguing against primitive duality.

It is conceivable in view of the evidence on both sides, that both schools may be right, that in some cases there are two amnions from the beginning and in others,



Fig. 3.—Fetal surface of the placenta showing absence of an amniotic partition.

there is but one. One of the many interesting conjectures presented in twin pregnancy is that of the origin of double monsters.

O'Schultze, quoted by H. H. Wilder¹¹⁷ grouped the types of twinning in man under four categories:

1. Two separate blastodermic vesicles with two deciduae reflexae and two placentas; this case is probably one in which there are two separate eggs, either from the same or opposite oviducts and implanted at some little distance from each other.
2. Two separate blastodermic vesicles inclosed in a single decidua, placentas fused with one another but with separate sets of umbilical vessels; this case is more frequent than (1) but apparently results from the same general cause, i.e., two separate eggs which are, however, implanted nearer together.
3. Two amnions and two umbilical cords with a single placenta, in the middle of which the two cords meet and upon which the umbilical vessels closely anastomose. These are inclosed in a single chorion and covered with a single decidua reflexa. The twins are always of the same sex.

4. Similar to (3) but with both embryos inclosed in a single amnion. *This is a very rare case*, explicable only by postulating a single blastodermic vesicle upon which the two embryonal areas are nearly or entirely in contact with one another. In such a case there would be an almost irresistible tendency toward the fusion of the two embryos, along the line of mutual contact, thus producing some form of composite monster.

The close connection of (3) and (4) suggests that many cases of compound monsters come under the same category as separate duplicates. This is quite probable but such forms arising from a secondary fusion would be more asymmetrical and more or less unequal and would come under the class of antosite and parasite rather than that of symmetrical or genuine double monsters.

Conjoined twins and double monsters are divided into two types, one in which the components or compound parts are equal to and the symmetrical equivalents of one another, Diplopagi, the Siamese type; the other, unequal and asymmetrical monsters, one component of which is smaller and dependent upon the other, autosite and parasite, sometimes the parasite is merely a head or head and arms attached to the autosite at or near the epigastrium or upper part of the abdomen.

There was in this collected series no true case of diplopagi found, which would argue against the condition of a single amnion in twin pregnancy as a cause for fusion to produce symmetrical monsters or diplopagi. However, Fischer³⁴ in 1866 advanced the theory that double monsters are the result of an early total fission of the embryo, followed by a secondary fusion of the parts. Wilder is inclined to endorse Fischer's theory. He says, "It will be remembered that in the account of intrauterine relations of duplicate twins, a condition was described in which the twins were not only monochorial but monoamniotic. This appears to me to present many possibilities for fusions."

Twinning carries with it hazards for one or both of the fetuses and the commonest cause is due to anomalous fetal circulation. Frederick Schatz³⁵ has probably written more upon the development of one-egg twins than any other observer. His material was extensive and his researches were published in the *Archiv für Gynaekologie* between the year 1882 and 1900. He says, as the result of an anatomical derangement or asymmetry of the vascular system, one of the twins is robbed of the blood supply necessary for its normal nourishment and functioning. The result is a progressive weakening of the heart with an accompanying decrease in size. The pressure of the blood from the strong opposite twin comes to bear upon this weakened heart and if sufficiently strong, overwhelms it and brings its rhythm to a standstill. This heart later atrophies. Life is maintained by the opposite or injured twin through what Schatz calls the third circulation, an anastomosis between the vessels of the respective twins in the placenta. Alfieri found in his collected series, several acardiac parasites and I found an additional one.

CLINICAL SIGNIFICANCE

The clinical significance concerns chiefly the fetuses for in all the cases reported, the delivery has not been more difficult than in any case of twin labor.

One might suppose that collision of the twins, that is, the simultaneous engagement of two presentations might complicate the delivery but in the cases already reported this has not happened.

Holzapfel says, "I consider it probable that by a collision of the twins, the partition is made to disappear." Here he refers to very early pregnancy. This pre-

supposes some opening in the amniotic partition *de novo*, through which collision might cause further tears and a disappearance of the remainder of the wall between the sacs. This does not sound plausible to the writer. Of the 109 cases here reviewed the period of gestation reached was as follows: full term 26, premature but viable (six and one-half to nine months) 25, nonviable 24, and not stated 34.

The chief clinical interest is the danger of death of one or both of the fetuses from twisting or knotting of the cords, which is very common.

In Roberg's⁸⁰ collected series there were 25 cases of twists and knots. Piltz⁸³ found 28 cases. In my review of 109 cases so far reported, torsion or true knot formation was reported 58 times or 53.2 per cent. In many of these the knots were multiple and so complicated that the knots could not be counted. Not only has this resulted in the death of one or both twins at or near full term but some of the early abortions were undoubtedly caused by this disturbance in the fetal circulation. The danger at delivery often arises from traction on the cord of the first twin, tightening the knots in the cord of the second, as in the case here reported, the cord of the first twin passing through many knots of the second. Bihler¹⁴ called attention to this danger to the second twin.

Dietrich's²⁷ experience and that of Hammerschlag⁴⁵ was practically identical with mine, that is, the cord of the second twin was caught in a knot of the first and the circulation cut off by the descent of the first twin. In the case reported by Newman⁷³ the midwife pulled upon the first cord, causing compression of the second. Podzahrodsky⁸⁶ relates an interesting complication where the midwife cut a cord tight about the neck of the first twin. It proved to be the cord of the second twin and only by a prompt delivery effected by Podzahrodsky were both twins saved.

Burger¹⁹ says, "For one or other of the children during the intrauterine life, no danger from twisting of the cords is likely to occur. Indeed, one found in each of the described cases, cord furrows on the umbilical cords." These are interpreted, according to Tarnier and Schauta and A. Martin as a postmortem change, "so that the danger of compression during uterine life does not seem to be great." This conclusion does not seem reasonable in view of the fact that abortion occurred in this series 15 times in which there was knotting or twisting. As proof against knotting and twisting of the cords is the length of the cords and the freedom of movement alive with knotted and twisted cords. The only explanation to be advanced for knotting and twisting of the cords is the length of the cords and the freedom of movement afforded by the presence of two fetuses in one sac. Samhammer⁹⁹ thought the twists came from shaking of the mother during a journey over a rough road.

Another suggestion is violent vomiting attacks. Müller experimenting with an artificial uterus and prepared fetuses produced twists by sudden violent shaking movements, but slight movements such as would occur in the living subject during pregnancy did not produce twisting or knotting.

PROGNOSIS

As indicated before, there is little or no risk to the mother in this condition. Although it might be expected, collision of twins during delivery did not occur. Eclampsia was mentioned four times and one mother died of central placenta previa. Neither of these complications could be ascribed to the fact that the twin pregnancy was monoamniotic.

For the fetuses, however, monoamniotic twinning is of serious import. Of the 109 authentic instances here reviewed, both twins survived in only 17 cases, a $15\frac{2}{3}$ per cent chance. Both twins died in 41 cases and one died in 20 pregnancies, there were 8 monsters to be added to the mortality column, in 23 cases the mortality was not stated, however, 8 of this number resulted in abortions, leaving 94 cases from which to estimate the mortality. Ninety-four twin pregnancies mean 188 babies, 126 did not survive, leaving a death rate of 68 per cent.

TREATMENT

Intelligent management presupposes a correct diagnosis. This is rarely made sufficiently early to be of value. If diagnosed after the birth of the first twin by the absence of a second rupture of the membranes, the second twin should be delivered immediately to prevent cord accidents, the usual cause of death.

SUMMARY

1. Monoamniotic twin pregnancy is of rare occurrence; only 109 authentic cases were found by me.
2. The prognosis for the fetuses is unfavorable as shown by a 68 per cent mortality.
3. The bad prognosis is due almost entirely to knotting and twisting of the umbilical cords.

BIBLIOGRAPHY

- (1) *Abe*: Jap. J. Obst. & Gynec. 12: 171, 1929. (2) *Abrams*: AM. J. OBST. & GYNEC. 1: 955, 1921. (3) *Adamson*: Edinburgh Obst. Soc. Trans. 22: 27, 1896. (4) *Ahlfeld*: Arch. f. Gynäk. 7: 210, 338, 1875. (5) *Alferi*: Ann. di ostet., Milano 25: 280, 331, 525, 1903. (6) *Ausch*: Frommels Jahresbericht 11: 762, 1897. (7) *Von Back*: Dissertatio de corde Roterodami, 1648, p. 45. (8) *Bailly*: Arch. de Tocologie, p. 490, 1882. (9) *Bumm*: Quoted by Roberg. (10) *Bar*: Bull. de la soc. d'obst. de Paris, p. 99, 1898. (11) *Bar*: Bull. Soc. d'obst. et de gynéc. de Paris 2: 771, 1914. (12) *Basso*: Zentralbl. f. Gynäk., No. 19, 1910. (13) *Bidoire*: Bull. Soc. d'obst. et de gynéc. de Paris, No. 3, p. 276, 1933. (14) *Bihler*: Zentralbl. f. Gynäk. 50: 1651, 1926. (15) *Boyd*: Ann. Gynec. & Pediat. Phila. 6: 10, 602; Jahrb. f. Geburtsh. u. Gynäk., p. 599, 1893. (16) *Boyer*: Contribution a l'étude des grossesses multiples dans une cavité amniotique unique, Thèse de Paris, N. 607 (Caso de Bar), 1897. (17) *Boissard*: Soc. d'Obst. de Paris 21: Nov., 1901; L'Obstetrique, No. I, p. 38, 1902. (18) *Breus*: Wiener med. Jahrbucher, p. 57 ff, 1882 (cit. da Schatz in Arch. f. Gynäk. 58: 61, 1899, Taf. LV, Fig. 41 ed. idem. 60: No. II, p. 201, 1900). (19) *Burger*: Zentralbl. f. Gynäk., No. 9, 1904. (20) *Busch*: Beschreibung zwei merkwürdigen menschlichen Missgeburt, Marburg, 1803. (21) *Caseaux*: Compt. rend. Soc. de biol. 3: 211, 1851. (22) *Coen*: Boll. sc. med. di Bologna 19: 29, 1887. (23) *Cornet*: Contribution a l'histoire des grossesses gemellaires, Thèse de Paris, p. 49, 1889. (24) *Crede*: Klin. Vortr. a. d. Geb., 1854. (Cit. by Kuster.) (25) *DaFoe*: Personal communication to the author, 1934. (26) *Diesterweg*: Mitt. d. Gesellsch. f. Geburtsh. in Berlin 5: 2 (Cit. ds Ahlfeldt). (27) *Dietrich*: Zentralbl. f. Gynäk., p. 586, 1914. (28) *DePuyt*: Verhandlingen uitgegeven door het zeeuwsh genootschap der wetenschappen te Vlissingen IX Deel, Middelburg, p. 426, 1762. (29) *Durieux*: Zentralbl. f. Gynäk., p. 438, 1890. (30) *Eastman*: J. Obst. & Gynec. 80: 343, 1919. (31) *Elben*: Arch. f. Gynäk. 58:

- 47, 1899. (32) *Eleuterescu*: Contribution a l'etude des grossesses multiples univitellines et bivitellines, Thésé de Paris, No. 244, 1896. (33) *Eustache*: Arch. de Tocol. et de gynéc., Par., p. 309, 1884. (34) *Fischer*: Quoted by Newman, H. H. (35) *Frankel*: Centralbl. f. Gynäk., No. 3, p. 33, 1883. (36) *Freund*: Ztschr. f. Geburtsh. u. Gynäk. 97: 100, 1930. (37) *Fricker*: Ueber Verschlingung und Knotenbildung der Nabelschnure bei Zwillingsfruchten. Tübingen, 1870. (Caso d. Dott. Haarer-Wurtemberg. Correspondenzbl. vom 1856.) (38) *Friedlander*: Monoamniotische Zwillinge, Berlin, Colmar, 1914. (39) *Garneri*: Mem. Acad. imp. d. Sc., Turin, p. 89, 1809-10. (40) *Geisler*: Ein Fall von Verschlingung der Nabelschnure bei Zwillingen in gemeinsamen Amnion, Inaug. Diss., Halle, 1898. (41) *Glaister*: Centralbl. f. Gynäk., No. 28, p. 493, 1889. (42) *Gueniot*: Schmidt's Jahrbucher 191: p. 51. (43) *Hauser*: München. med. Wehnschr., No. 15, p. 812, 1913. (44) *Hahl*: Monatschr. f. Geburtsh. u. Gynäk. 16: p. 794. (45) *Hammer-schlag*: Deutsche med. Wehnschr. 5: 190, 1900. (46) *Heil*: Fortschr. d. Med. Berlin 38: 346, 1921. (47) *Hermann*: Arch. f. Gynäk. 40: 253, 1891. (48) *Hillier*: Indian Med. Rec., Calcutta 13: 233, 1897. (49) *Hink*: Centralbl. f. Gynäk., No. 27, p. 724, 1898. (50) *Hofmeier*: Die menschliche Placenta, Wiesbaden, 1890. (51) *Holzappel*: Beitr. z. Geburtsh. u. Gynäk. 8: 1, 1904. (52) *Howarth*: Zentralbl. f. Geburtsh. u. Gynäk. 36: 1033, 1912. (53) *Hyrtl*: Arch. f. Gynäk. 24: p. 383, Pl. D. (54) *Jeannin*: Presse med. 14: 645, 1906. (55) *Jaggard*: Am. J. Obst. 19: 1180, 1886. (56) *Jenot*: Arch. de tocol. et de gynéc., Par., p. 408, 1886. (57) *Jonkoff*: Ueber einen Fall von monoamniotischen Zwillingen mit insertio velamentosa funiculi umbilicalis, Heidelberg, Strasbourg, 1926. (58) *Jorg*: Kohlscutter, Inaug. Diss., Leipzig, p. 32, 1833. (59) *Kehrer*: Ann. de Gynéc. 27: 56, 1887, and Centralbl. f. Gynäk., No. 41, p. 665, 1886. (60) *Kleinwachter*: Die Lehre von den Zwillingen, Prag., p. 95, 1871. (61) *Kouwer*: Zentralbl. f. Gynäk., No. 16, 1905. (62) *Krunkenberg*: Ztschr. f. Geburtsh. u. Gynäk. 22: 465, 1891. (63) *Langlet*: Union Med. et Sc. du Nord-Reims 1: 120, 1877. (64) *Lind*: Ueber Zwillingschwangerschaft und deren Verlauf. Inaug. Diss., Berlin, p. 27 (Fall 95), 1868. (65) *Mannel*: Arch. f. Gynäk. 10: 388, 1876. (66) *Mayer*: Verhandl. der Geburtsh. Gesellsch. zu Berlin, Erster Jahrgang, p. 132, 1846. (67) *Mery*: Mem. Académie de Paris 10: p. 324, 1666-99. (68) *Mery*: Mem. Acad. roy. d. Sci. Année DCCXX, p. 8, Paris. (69) *Maygrier*: Jahrb. f. Geburtsh. u. Gynäk., 1908. (70) *Moreau*: Bull. Soc. anat. de Par., p. 116, 1860. (71) *Müller*: Ueber Verschlingung und Knotenbildung der Nabelschnure bei Zwillingsfruchten. Tübingen, 1870. Correspondenzbl. Juli 1, 1856, Caso del Dott. Haarer, Wurtemberg. (72) *Müller*: Beiträge zur Statistik der mehrfachen Schwangerschaft. Inaug. Diss. Jena, p. 15, 1889. (73) *Newmann*: Edinburgh M. J. 2: 8, 1858. (74) *Newman, H. H.*: Physiology of Twins, Univ. Chicago Press, 1923; Biology of Twins, Univ. Chicago, 1917. (75) *Niemeyer*: Ztschr. f. Geburtsh. u. prakt. Med. 8: 189, 1828. (76) *Noll*: Ein Fall von Verschlingung und Umschlingung der Nabelschnure bei Zwillingen in gemeinsamen Wassersack. Inaug. Diss., Marburg, 1889. (77) *Opitz*: Centralbl. f. Gynäk., No. 12, 333, 1899. (78) *Osiander*: Epigrammata in diversas Musei sui anatomici, p. 30, Gottingen, 1814. (79) *Osterloh*: Zwillinge mit Nabelschnurverschlingung. Geburtshilfliche Gesellschaft, Dresden, 15 Okt., 1903. Monatschr. f. Geburtsh. u. Gynäk. 19. (80) *Pallin*: Zentralbl. f. Gynäk. 31: 1579, 1907. (81) *Patti*: Rassegna d'ostet. e ginec. 39: 655, 1930. (82) *Pfeilstriker*: Zentralbl. f. Gynäk. 29: 1499, 1905. (83) *Piltz*: Zentralbl. f. Gynäk., p. 38, 1907. (84) *Parsons*: (85) *Pirvass*: Zwillinge in einer Amnionhöhle, Leipzig, 1906. (86) *Podzahrodsky*: Wien. klin. Wehnschr. 25: 413, 1912. (87) *Reynolds*: Am. J. M. Sc., No. 31, 1835. Cited by Ahlfeld. (88) *Resenilli*: Quoted by Jeannin. (89) *Roberg*: Trans. Chicago Path. Soc. 8: 83, 1909-10. (90) *Sachs*: Ztschr. f. Geburtsh. u. Gynäk., Stuttg. 86: 197, 1923. (91) *Schatz*: Arch. f. Gynäk. 55: 555, 1898. (92) *Schatz*: Archiv. f. Gyn., 1884, Bd. 24, Hft. 3, s. 377. (93) *Idem*: Arch. f. Gynäk. 58: Fig. 47. (94) *Schroter*: Wurtemb. Korrr. 33: 1857; bei Ahlfeld, Arch. 7: p. 269. (95) *Schulein*: Ztschr. f. Geburtsh. u. Gynäk. 8: 194. (96) *Schroeder*: Wurtembergisches Correspondenzblatt 33, 1857. (97) *Schultz*: Quoted by Wilder. (98) *Scoscia*: Progresso medico, 1892, N. 15. (99) *Sammhammer*: Rust Mag. f. d. ges. Heilk. 19: 48, 1825. (100) *Siebold*: Monatschr. f. Geburtsk. 14: 419, 1859. (101) *Sedlaczek*: Arch. f. Gynäk. 26: 309, 1885. (102) *Sippel*: Ein menschlicher Acardiacus. Inaug. Diss., Marburg, 1875. (103) *Soete*: Gaz. hebdom. de méd. 1: 226, 1853-54. (104) *Sonntag*: Ein Fall Verschlingung und Knotbildung der Nabelschnure bei Zwillingen in gemeinsamen Amnion, Diss., Leipzig, 1905. (105) *Spaeth*: Ztschr. d. Wien. Gesellsch. d. Aerzte, No. 15, 16, 1860. (106) *Stein*: Siebold's Lucina 111: 25, 1805. (107) *Strassman*: Ztschr. f. Geburtsh. u. Gynäk., p. 1717, 1913.

- (108) *Sygmundin*: Brandenburgische Wehmutter, Berlin, 1689; cited by Taruffi. (109) *Simpson*: Zentralbl. f. Gynäk. 21: 680, 1897. (110) *Tiedeman*: Sieboldt's *Lucina* 111: 19, 1805. (111) *Trautner*: Ueber monoamniotische Zwillinge (Erlanger), München, 1915. (112) *Underhill*: Zentralbl. f. Gynäk., p. 24, 1877. (113) *Fallos*: Bull. et mém. Soc. d'anthrop. de Paris 4: 213, 1913. (114) *Weiss*: Cited by Hink. (115) *Wenzel, G.*: Zentralbl. f. Gynäk., No. 22, 1904. (116) *Wenzel, Th.*: Zentralbl. f. Gynäk., No. 32, 1905. (117) *Wilder*: Am. J. Anat. 3: 384, 1904. (118) *Williams, T. J.*: AM. J. OBST. & GYNEC. 21: 129, 1931. (119) *Williams, J. W.*: Textbook on Obstetrics, New York, 1927, D. Appleton Company, p. 406. (120) *Winslow*: Philadelphia Med. Times 47: July, 1872. Arch. f. Gynäk. 7: 266, 1875. (121) *Winckel*: Lehrbuch der Geburtshilfe, I Auflage, p. 443, 1889; II Auflage, p. 417, 1893. (122) *Wolf*: Zwei neue Falle monoamniotischer Zwillinge, Leipzig, 1920. (123) *Ygonin*: Gaz. med. de Lyon, No. 13, 1864.

26 SOUTH GOODMAN STREET

THE "COLD TEST" IN PREGNANCY*

A PRELIMINARY REPORT OF ITS USE IN PRENATAL CARE

LAWRENCE M. RANDALL, M.D., STEPHEN E. MURRAY, M.D., AND
ROBERT D. MUSSEY, M.D., ROCHESTER, MINN.

(From the Mayo Clinic)

WAGENER has shown that changes in the retinal arterioles usually keep pace with increase in hypertension in cases of toxemia of the latter months of pregnancy. The first change is narrowing of the lumens of the arterioles, resulting from spasm or spastic constriction. As the toxemia and blood pressure increase, this constriction may become fixed, and in the retina occur other changes which are recognized as characteristics of the retinitis of the toxemia of pregnancy. The initial retinal changes suggest that the normal balance of the autonomic nervous system has been disturbed, and that vasomotor imbalance of the entire arteriolar bed has occurred.

Evidence indicates that an incipient rise in blood pressure is the earliest sign of beginning preeclamptic toxemia, and the severity of the toxemia is usually considered to be in direct relation to the degree of hypertension. Exceptions occur, however. It would be advantageous, if by some test it might be possible to determine the presence of vasomotor imbalance before onset of the usual symptoms of toxemia of pregnancy or at least to determine with what frequency this vasomotor imbalance occurs during pregnancy.

Hines and Brown, in studying the subject of hypertension from the standpoint of the internist, devised a type of standard stimulus whereby the pattern of reaction of the vasomotor system could be determined. This is known as the "cold test," and the technic of it is as

*Read at the Forty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, White Sulphur Springs, W. Va., September 6, 7, and 8, 1934.

follows: The subject remains recumbent for fifteen minutes, or until the blood pressure has attained or approximated the basal level. In cases of hypertension as long as forty-five minutes may be required. With the cuff of the sphygmomanometer placed on one arm, the hand on the opposite side is placed in water that is at a temperature of 4° to 5° C.; the blood pressure is taken at the end of thirty seconds and again at the end of sixty seconds. The hand is removed from the water and readings are taken every two minutes until the blood pressure has returned to its previous basal level. The highest reading obtained is recorded as the measure of the response.

The originators of the test reported that there is a response of both systolic and diastolic pressure, but that the response of the latter is somewhat less than that of the former, and is more variable. They considered that the response to cold has a purely reflex basis, because

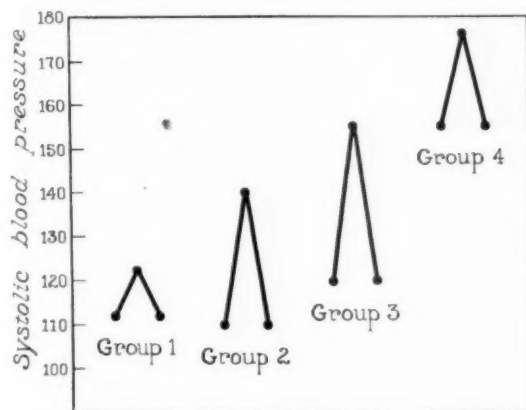


Fig. 1.—Response to cold test. The groups are described in the text, and are designated briefly in Table I.

the reaction is so rapid that any known hormonal or chemical factor could not be concerned. A tourniquet, producing stasis of the flow of blood in the arm that is immersed, fails to inhibit the reaction.

Hines and Brown did not apply their test to pregnant women, but we thought that it should be applied, in the prenatal period, to a sufficient number of patients to prove or disprove its value in forecasting preeclamptic toxemia.

MATERIAL AND RESULTS

Reactions to the cold test, numbering 130, were determined on 104 pregnant women who were divided into five groups. Results in four of the groups are given in Table I and Fig. 1. Composition of the groups was as follows:

Group 1.—Among the sixty-five women in this group, no evidence of toxemia of pregnancy had appeared by the time of performance of the tests represented in

Line 1 of Table I, nor had such signs appeared at the time of writing of this paper. These women gave normal responses to the tests.

Hines and Brown found a mean rise of systolic pressure of 8.62 mm. of mercury and a mean rise of diastolic pressure of 8.14 mm. of mercury in studies of the normal male and of the normal, nonpregnant female. They considered 15 mm. of mercury as the maximal rise for normal persons, for the range of their readings in this group was between 5 and 15 mm. of mercury. The range in our normal group was slightly higher, so that we accepted 20 mm. of mercury as the maximal reaction of the normal female in the prenatal period.

TABLE I. RESPONSE OF PREGNANT WOMEN TO COLD TEST OF HINES AND BROWN

GROUP		PATIENTS	BLOOD PRESSURE, MM. OF MERCURY			
			MEAN RISE		MEAN BASAL	
			SYSTOLIC	DIASTOLIC	SYSTOLIC	DIASTOLIC
1	Normal response to test; no toxemia to time of writing of paper	65	10.3	10.7	112	67
2	Exaggerated response to test; no toxemia to time of writing of paper	14	30.0	22.5	110	65
3	Exaggerated response to test; toxemia between time of performance of test and time of writing of paper*	7	35.2	26.0	120	77
4	Toxemia at time of performance of test*	8	21.0	10.0	155	94

*Four of the patients included in this group were also included in the other group indicated by an asterisk. Results with fourteen other patients are recorded in the text. Thus the total of patients was 104.

Group 2.—None of the fourteen women in this group had given evidence of toxemia of pregnancy by the time of performance of the tests represented in Line 2 of Table I, nor had such signs appeared at the time of writing of this paper, even though one of the patients had been confined. The patients, however, did give exaggerated responses to the tests.

Group 3.—Among the seven women of this group, no evidence of toxemia of pregnancy had appeared by the time of performance of the tests represented in Line 3 of Table I, but all of the seven women had given signs of toxemia before the time of writing of this paper. These patients also gave exaggerated responses to the tests. Of three of these seven patients, reactions when first determined, were within normal limits, but they became exaggerated later in pregnancy, before onset of the signs of toxemia.

Group 4.—The eight women in this group had given signs of toxemia of pregnancy before the time of performance of the tests represented in Line 4 of Table I.

We are not prepared at present to try to evaluate the reaction to the cold test of patients, such as these in this group, who have toxemia of pregnancy at the time the test is performed.

Group 5.—A group of fourteen patients who gave no symptoms of toxemia, reacted in a manner which does not correspond to any of the reactions obtained by Hines and Brown. This reaction consisted in a persistent fall from the basal levels, of both systolic and diastolic pressures, during the period of immersion of the hand in cold water. In some of these cases, the fall persisted after removal of the hand, and in others the pressures rose to approximate the basal levels within two minutes. In two cases in which fall of the blood pressure was persistent, there was an asso-

ciated sense of faintness, which disappeared as the blood pressure rose. This represents essentially an inverted reaction for which we have no explanation at present. Swelling of the immersed hand, or other symptoms which might be associated with cold allergy, did not appear. The symptoms related may be as significant of vasomotor imbalance as is the exaggerated reaction of blood pressure but so far none of this group of fourteen patients has shown any signs of toxemia of the latter months of pregnancy. The basal blood pressures were 117 mm. of mercury systolic, and 75 mm. diastolic. The mean fall in systolic pressure was 11.2 mm. of mercury and that of the diastolic pressure was 6 mm.

COMMENT

In attempting to apply this standard test of measuring the variability of blood pressure in the prenatal period, the only values we have for comparison deal with the general problem of hypertension. Although the exact cause of elevation of the blood pressure is not yet determined, it is felt that the hypertension associated with toxemia of the latter months of pregnancy is related to a toxin which affects the whole maternal organism. We have evidence that preeclamptic toxemia is associated with spastic constriction or with contraction of the arteriolar system, through observations made on the arterioles of the retinas of patients suffering from this condition. This constriction or contraction may be related to a particularly reactive vasomotor system. It is possible that a pregnant woman who manifests an exaggeratedly reactive vasomotor system in response to the cold test is more likely to suffer from toxemia of the latter months of pregnancy. It is significant that in no case in which the response to the cold test has been persistently normal, has toxemia developed, and that in all cases in which toxemia has developed a hypertensive reaction has been demonstrated.

Of the patients who have manifested a definitely exaggerated reaction (Groups 2 and 3, Table I), 33 per cent have presented the usual signs of toxemia in the latter months of pregnancy.

This paper is presented as a preliminary report. More studies are to be made on the patients already under observation and the number of patients is to be enlarged.

REFERENCES

- (1) *Hines, E. A., Jr., and Brown, G. E.*: *Ann. Int. Med.* 7: 209, 1933. (2) *Wagener, H. P.*: *J. A. M. A.* 101: 1380, 1933.

Estes, Jr., and Heitmeyer: *Pregnancy Following Ovarian Implantation*, *Am. J. Surg.* 24: 563, 1934.

After bilateral salpingectomy an ovarian implantation had been done in which the cut surface of the ovary, still attached to its pedicle, was implanted upon the cut surface of the uterine horn. Of 50 patients operated upon in this manner, whose records are complete, four (8 per cent) became pregnant, two had abortions at about the third month and two had full-term pregnancies.

J. THORNWELL WITHERSPOON.

THE USE OF PARALDEHYDE IN OBTAINING OBSTETRIC ANALGESIA AND AMNESIA*

HOWARD F. KANE, A.B., M.D., F.A.C.S., AND GEORGE B.

ROTH, A.B., M.D., WASHINGTON, D. C.

(From the Department of Obstetrics and Gynecology and the Department of Pharmacology, George Washington University)

EACH of the existing methods of obtaining analgesia and amnesia during labor has some objectionable features. Ether mixtures tend to cause asphyxia of the baby. Barbiturates usually produce amnesia only; the fact that there is little or no actual pain relief is shown by the marked restlessness which attends each uterine contraction. Scopolamine is a drug of high toxicity, is not analgetic, and only in combination with other drugs is it sufficiently powerful to produce amnesia.

Drugs administered hypodermically are beyond control once they are given. Oral medication is frequently impossible because of the tendency of patients to vomit during labor. Many solutions designed for rectal instillation are not well retained as they cause irritation of the mucosa.

The procedures which will be described in this paper are the results of repeated pharmacologic experiments and clinical tests performed in an attempt to secure relief and forgetfulness of pain by the use of drugs of the lowest toxicity, drugs which cause the least excitability and are the least likely to cause harm to mother or child.

The flexibility and wide safety range of paraldehyde suggested its employment as the basic factor around which the technic might be developed. Rectal administration was chosen, as the solution may thus be given to an unconscious patient. In order to facilitate retention of the paraldehyde, the rectal mucosa is anesthetized by the addition of benzyl alcohol. As benzyl preparations have the power to relax unstriated muscle, it was believed that it would allow more rapid dilatation of the cervix. Laboratory and clinical observations have seemed to prove that this is true.

Paraldehyde is not a complete analgesic as pain impulses evidently reach the brain even though the patient be unconscious. In our early cases we attempted to block pain conduction by giving amidopyrine intramuscularly, but the results did not warrant its continuation. An occasional dose of morphine will augment the action of paraldehyde

*Read at the Forty-Seventh Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., September 6, 7, and 8, 1934.

when proper analgesia is not being obtained. Opium derivatives are said to be particularly dangerous to the fetus through depression of the respiratory centers. Personal experience with morphine, however, has convinced us that the incidence of asphyxia caused by this drug is grossly exaggerated.

Resenstein and Davidoff, Bartholomew and others have found paraldehyde to be of value in relieving the pain of labor, but they have used it in connection with various barbiturates, a group of drugs which we have avoided because of our belief that they are dangerous in the dosage required.

In addition to the clinical observations to be reported in this paper, experiments upon the uteri and cervixes, extirpated and in situ, of several species of laboratory animals have been made. A detailed account of this work, from a pharmacologic viewpoint, will be published in a future communication, but at this time only the clinical results will be presented.

Disregarding the first twenty or thirty cases in which we were endeavoring to learn the optimum dosage and technic, we offer our observations in a series of 175 cases of labor in which the method has been employed.

TECHNIC OF ADMINISTRATION

At the beginning of labor, the rectum is emptied by a soapsuds enema, followed by tap-water irrigation until the return is clear. This is a particularly important step in the technic. In five cases excitement was present to the point of requiring restraint. In each case it was found that the rectum contained a large amount of fecal matter which undoubtedly interfered with the absorption of the solution.

As soon as the patient says that the contractions are painful, regardless of the state of the cervix or the interval between pains, the treatment is started.

The most satisfactory dose of paraldehyde has been found to be 1 c.c. to each 8½ pounds of the patient's weight. For practical purposes it is sufficiently accurate to give 1 c.c. to each 10 pounds and add 2 or 3 c.c. To the paraldehyde is added 1.5 c.c. of benzyl alcohol. This mixture is instilled into the rectum by gravity through a large catheter and is followed by one ounce of salt solution to wash it out of the tube. If the patient is not asleep in thirty minutes, ¼ gr. of morphine is given hypodermically. Should the patient be awake one hour after the morphine injection, the original dose of paraldehyde and benzyl alcohol is repeated. Usually, however, the rectal medication need not be repeated for several hours. The patient sleeps soundly, perhaps stirring with each pain. In many cases the only evidence of uterine activity is the seeing or feeling of the contractions by the observer. As the effect of the drugs begins to wear off, the patient becomes slightly restless and may complain of discomfort but falls asleep immediately after each pain. At this time the rectal injection is repeated. The effect of each dose lasts from two to five or six hours, three hours being the average duration. Occasionally, when the repeated dose does not give prompt results, ¼ gr. of morphine is given fifteen to thirty minutes later. When the presenting part reaches the perineum, delivery is accomplished by outlet forceps under ethylene anesthesia.

The objects sought for in the use of these procedures are analgesia and amnesia without endangering mother or child, adding to the length of labor or causing undue excitation of the patient.

Evaluation of results shows that the degree of success varies with the length of labor. In the case of a multipara in labor only for one or two hours, this method of treatment is practically useless; to the primipara with a slowly progressing posterior position it is a very great relief.

In estimating the length of labor, it has been necessary to disregard the usual division into first and second stages. In most instances one stage merges imperceptibly into the other, and frequently the bulging perineum has been the first indication of full dilatation of the cervix. Observation of these cases has strengthened our belief that the voluntary contractions of the abdominal muscles are of no great importance in the second stage of labor. We have practically abandoned the practice of having the patient "bear down" and pull on straps. For the perineal stage, anesthesia is necessary. In this series, ethylene has been used in the majority of cases. When it has been impossible to secure the services of an experienced anesthetist, ether has been given.

As it is our custom to deliver by outlet forceps practically all heads that reach the perineum, to rotate and deliver all posterior occiputs if progress ceases for one hour and to extract all breeches when the cervix is dilated, our operative incidence has not been increased. As the patient is unconscious and therefore cannot cooperate, instrumental aid at the perineal stage is practically always necessary.

The patients usually sleep soundly for six or eight hours after delivery. No ill effects on the mother have been noted. The pulse rate, blood pressure, and respirations remain unchanged. Urinalysis has shown no kidney damage. While no case of serious cardiac disease has been found in this series, several patients with symptomless murmurs have been carried through labor with complete success. Toxemia, nephritic or hepatic, seems to be no contraindication to the use of this method, as several cases of this type showed no ill-effects. Postpartum bleeding has not been increased. Records of animal experiments in the laboratory have confirmed these clinical observations.

When ethylene has been used during delivery, the babies have breathed and cried as promptly as in cases where no analgesic agent had been employed. Several cases of delayed breathing but not dangerous asphyxia have occurred when it had been necessary to use ether for delivery.

In the laboratory it was learned that paraldehyde slightly decreased the force of uterine contractions and that benzyl alcohol seems to relax the cervix. As the average labor in this series was much shorter than the accepted normal figures, it would seem that the softening of the cervix more than offsets the diminution in power of the contractions.

The results in regard to analgesia and amnesia separate the cases into four groups. Group A consists of cases in which analgesia is considered to have been adequate and amnesia complete. The patients in Group B are those who move about and complain of pain. Many of these patients seem to be entirely rational at times. Amnesia, however, in this group is complete. Patients who remember having had pain, but who have undoubtedly been markedly relieved, constitute Group C. In Group D are those who received no benefit whatever.

Of 94 primiparas, 59 are in Group A, 29 in Group B, 3 in Group C, and 3 in Group D. Of 81 multiparas 32 are in Group A, 29 in Group B, 11 in Group C, and 9 in Group D. All of the patients in Group C were in labor less than four hours and those in Group D less than two hours. The duration of labor as estimated from the time of the first dose of the rectal solution until delivery was started varied, in primiparas, from one to thirty-eight hours. Labor in multiparas lasted from one-half to fourteen hours. Sixty-seven, or 71 per cent, of the primiparas and 68, or 34 per cent, of the multiparas were in labor less than ten hours. From one to six rectal injections were given, the average number being two in primiparas and one in multiparas. Morphine was used at the beginning of labor in 122 cases and was repeated in 48.

TABLE I

	GROUP A AMNESIA AND ANALGESIA	GROUP B AMNESIA AND PARTIAL ANALGESIA	GROUP C PARTIAL AMNESIA AND ANALGESIA	GROUP D LITTLE OR NO RELIEF
Primiparas	59	29	3	3
Multiparas	32	29	11	9
Total	91	58	14	12

CONCLUSIONS

1. The combination of paraldehyde and benzyl alcohol produces satisfactory analgesia and complete amnesia in practically all cases in which labor is of more than four hours' duration.

2. This solution is retained, having been expelled only in cases in which the presenting part was pressing on the rectum. It does not cause vomiting.

3. No ill-effects have been noted in either mother or child.

4. Having been spared the psychic shock of pain, the memory of suffering and fatigue from bearing down and straining during the second stage, the patient awakens from her long postpartum sleep actually refreshed.

5. The method here described is not perfect, but it seems to accomplish more with fewer disadvantages, than any other of the existing methods of relieving the pains of labor.

A STUDY OF CARCINOMA OF THE CERVICAL STUMP DEVELOPING AFTER SUBTOTAL HYSTERECTOMY*

WILLIAM P. HEALY, M.D., F.A.C.S., AND A. NORMAN ARNESON, M.D.,
NEW YORK, N. Y.

(From the Memorial Hospital)

THE occurrence of carcinoma as a primary lesion in the cervical stump after subtotal hysterectomy was first mentioned by Chrobak¹ in 1896. The earliest attempt toward a more comprehensive study upon this subject was the work of Condamin,² whose publication appeared in 1902.

Gilbert,³ Hochman,⁴ and others have reported that carcinoma develops in the cervical stump of 0.3 per cent to 2 per cent of the patients subjected to supra-cervical hysterectomy. The low incidence would not justify the greater mortality rate of total hysterectomy as a generally accepted routine. However, complete removal may be indicated in patients presenting badly lacerated or inflamed cervixes with some other lesion of the corpus. The importance of careful diagnosis before operation is illustrated by the combined statistics of Schottlander, Spencer, and Noble, reported by Polak.⁵

The difficulties encountered in the treatment of patients with carcinoma of the cervical stump and the poor results invariably reported by all authors, have also been responsible for the active interest displayed in this problem. The anatomical distortion due to the previous laparotomy has rendered adequate surgical removal extremely hazardous. This has in general relegated the treatment of these patients to radiation. The poor results obtained from radiation have been attributed to the absence of the uterine corpus, which may prevent a correct application of radium for a sufficient dose. It has been intimated that as a result of faulty applications normal tissues are frequently overirradiated, and that peritoneal accidents are apt to occur. The absence of the uterine corpus would not seem to increase materially the complications from external irradiation. Healy⁶ has repeatedly emphasized the importance of roentgen irradiation for the treatment of parametrial disease, and he has pointed out that an adequate dose of radium applied to the cervix is capable of controlling the disease only in and directly adjacent to the cervix. In the statistical reports that have been published upon the treatment of carcinoma of the cervical stump, sufficient external irradiation has seldom been employed.

*Presented before the Section on Obstetrics and Gynecology, New York Academy of Medicine, November 28, 1933.

To classify any patient as one in whom carcinoma developed in the cervix after the uterine corpus had been removed, one must ascertain whether or not disease was present at the time supracervical hysterectomy was performed. It is impossible to be completely informed as to the clinical and histologic appearance of the cervix at the time of previous operation in each suspected instance. The time factor, therefore, must serve as the criterion of selection. That is, the interval elapsing between the removal of the uterine corpus and the development of carcinoma must be sufficient to remove all reasonable doubt that a malignant tumor was not present at the time of operation. Upon this basis the cases selected for this series were those in which at least one year elapsed following operation before symptoms of cervical carcinoma appeared, or in which at least three years elapsed before the diagnosis of carcinoma was made.

Zampa⁷ states that the incidence of stump carcinoma among all patients with malignant disease of the cervix has been variably reported from 0.2 per cent to 4 per cent.* Among the 2,600 patients admitted to the Gynecological Clinic of Memorial Hospital from January, 1920, to July, 1933, with the diagnosis of carcinoma of the cervix, 67 pa-

*Since the presentation of this paper, von Graff (AM. J. OBST. & GYNEC. 28: 18, 1934) has published a comprehensive report upon carcinoma of the cervical stump. In a collected series of 4,269 patients with cervix cancer he found the average incidence of stump cancer to be 4.1 per cent. However, in some of the individual clinics that were quoted, the incidence was much greater, and von Graff believes that carcinoma of the cervical stump may occur more frequently than is commonly recognized. The material he reported included patients in whom carcinoma was present at the time of subtotal hysterectomy, as well as those in whom carcinoma developed as a primary lesion in the cervical stump after removal of the uterine corpus. Of 551 patients upon whom there was sufficient data, 23.5 per cent had carcinoma of the cervix at the time of operation. He presents a plea for total hysterectomy as a prophylactic measure, because most stump cancers are epidermoid in character, and destruction or removal of the cervical mucosa by coning out, etc., has failed to prevent its occurrence. He also states, that "properly performed, both in the literature and my own experience testify that the operative mortality is not considerably higher."

Pearse (Surg. Gynec. Obst. 58: 845, 1934) contends that the possibility of carcinoma developing in the cervical stump should not be considered as an indication for total removal of the uterus, unless the mortality for this operation can be shown to be the same or less than for supravaginal hysterectomy. He reported an operative mortality of 1.7 per cent among 1,900 patients upon whom subtotal hysterectomy had been performed. Pearse also published statistics that have been quoted by von Graff, as well as those from other clinics, as follows:

	PERCENTAGE OPERATIVE MORTALITY	
	TOTAL HYSTEREC- TOMY	SUBTOTAL HYSTEREC- TOMY
Weibel	3.55	4.25
Amreich	3.8	1.7
Shaw	5.9	3.05
Fullerton and Faulkner	4.1	4.4
Masson	1.3	1.8
Mayo	1.8	1.2
Burch and Burch	3.1	4.2
Bartlett and Simmons	5.1	

Of the 1,900 patients from whom the uterine corpus had been removed, Pearse was able to trace 810 for a period of five or more years. The incidence of stump carcinoma among the patients who were followed was 1 per cent.

The average of the collected statistics quoted by von Graff revealed that 0.62 per cent of patients treated by subtotal hysterectomy developed carcinoma in the cervical stump at some later date. The greater incidence of stump carcinoma among all cases of cervix cancer is undoubtedly due to the failure of recognizing the presence of the disease at the time of operation. Von Graff has stated, that among the patients upon whom he had sufficient data, 23.5 per cent had carcinoma of the cervix at the time subtotal hysterectomy was performed.

tients, or 2.6 per cent of the entire number, were found who had developed malignant disease in the cervical stump. From three to ten years intervened between subtotal hysterectomy and the diagnosis of carcinoma in 48 per cent of the cases, and from ten to twenty years in 37 per cent. In 15 per cent the disease was not recognized until twenty to thirty-seven years after laparotomy.

TABLE I. NUMBER OF YEARS INTERVENING BETWEEN SUBTOTAL HYSTERECTOMY AND THE DIAGNOSIS OF CARCINOMA IN THE CERVICAL STUMP

	YEARS AFTER SUBTOTAL HYSTERECTOMY			
	3 TO 10	10 TO 20	20 TO 30	30 TO 37
Number of patients	32	25	7	3
Percentage	48	37	10.5	4.5

A survey of this group of 67 patients shows them comparable in age, clinical extent of disease, histologic grouping, and symptomatology with the other cases of cervical carcinoma reported by Healy.

The extreme age limits were twenty-three and sixty-seven years. Thirty-six per cent of the patients were between forty and fifty years of age, and 42 per cent were found to be from fifty to sixty years old.

There were 18 patients, or 27 per cent of the series, who were classified as having early or borderline disease, forming a group with a favorable prognosis. Forty-nine patients, or 73 per cent, had advanced lesions, and presented an unfavorable prognosis.

Histologic diagnosis had been made in all of the 67 patients except two. One of these applied to the clinic in a condition too far advanced for treatment, having already developed a vesicovaginal fistula. The other patient survived three years after treatment and died of carcinoma metastases and pelvic peritonitis. Among the 65 patients with histologic data 61, or 94 per cent, were epidermoid in type. Four patients, or 6 per cent, were found to have glandular carcinoma. Of the epidermoid lesions 18 per cent were classified as Group I, 72 per cent as Group II, and 10 per cent as Group III.

Monod⁸ reports a preponderance of the glandular variety of carcinoma among those patients developing carcinoma in the cervical stump within a short time after removal of the corpus uteri. This would seem to indicate that malignant disease had been present at the time of operation, and was probably located in the endometrium. The four cases of adenocarcinoma included in the series reported here were diagnosed six, sixteen, nineteen, and thirty years after hysterectomy. This long interval between operation and the recognition of adenocarcinoma in the cervical stump indicates that the disease had developed in the cervical glands, or remaining lower uterine segment after removal of the corpus. This further substantiates the contention that as far as can be determined, the patients included in this series

represent cases in whom primary carcinoma developed in the cervical stump after subtotal hysterectomy.

The clinical symptoms for which the patients presented themselves were identical to those usually noted in carcinoma of the cervix. Bleeding and actual hemorrhage were present in 74 per cent. Bloody discharge was noted in 24 per cent, and leucorrhea alone occurred in 2 per cent. Pain was a rather conspicuous feature among the patients with an unfavorable prognosis. It was usually located in the lower back over the sacrum, and radiated into the hips.

It might be supposed that patients who had already undergone surgical treatment for a major pelvic disorder would report for medical attention promptly after the occurrence of gynecologic symptoms. This was not found to be true in this series however, since the patients did not present themselves for treatment any earlier than other cases of cervix carcinoma. In a review of 100 patients with cervix cancer, 65 per cent received treatment within a year after they first observed symptoms of an intravaginal disturbance. Sixty per cent of the stump cases were seen within a year after the onset of symptoms. The importance of educating the public to seek medical advice upon the appearance of unusual signs or symptoms cannot be overestimated in the attempt to control cancer.

Pinsan⁹ states that in most cases of carcinoma of the cervical stump, subtotal hysterectomy has been performed for fibromyomas. This is to be expected since a large percentage of corpus amputations are done for the removal of myomatous uteri. In our series 58 per cent of the patients had been operated upon for this condition. Other indications for previous surgery were, bleeding uteri, pelvic inflammatory disease, benign ovarian disorders, and prolapse of the uterus. These data afford no additional information concerning the etiology of carcinoma developing in the cervical stump.

Polosson¹⁰ and Monod⁸ have suggested the possibility that resulting alteration in the physiologic and anatomical conditions caused by operative interference may predispose tissues of the cervical stump to the development of carcinoma. An isolated cervix is often seen to undergo regression in size and to assume senile characteristics. However, it is impossible to state whether or not this has any influence upon the development of malignant tumors. It has been generally agreed that carcinoma of the cervix is associated with multiparity. The high incidence of fibromyomas and the history of other pelvic disorders in all of the patients in this series, suggest that sterility may have existed in some of the patients. All of the patients were married, but 9 per cent had never been pregnant. As nearly as could be determined from the available data, about 85 per cent had been delivered between midterm and term. In a similar study of 46 patients Branscomb¹¹ found that only 80 per cent had borne

children. In all cervix cases from 90 to 94 per cent of the patients have a history of preceding childbirth.

Monod⁸ states that less than 15 per cent of all patients with carcinoma of the cervical stump are cured. He believes that the best statistics so far published have come from the Institut du Radium in Paris. Among the 27 patients observed at that institution, 10 were reported living for two to ten years after treatment.

At the Memorial Hospital all of the patients have been treated by radiation except three, who received no treatment because of their hopeless prognosis. Examination of the yearly survival in the 64 treated patients shows that the best results have been obtained over the past seven or eight years. This may be due to the fact that high voltage roentgen ray was used in addition to radium in most instances.

From 1929 to the present time 28 patients have been treated. The yearly survival among these patients has been sufficiently improved to indicate that a greater total salvage may be obtained. The prospects of better results in this group may be attributed to the greater amount of external irradiation which the patients have received. The roentgen ray cycle administered before the radium treatment was given has been particularly important. By this means the cervix has been better prepared for the application of radium, because the infection is diminished, and regression of the lesion lessens the trauma of placing radium within the canal.

The five-year salvage of the 36 patients who were treated five or more years ago is 14 per cent. This result compares favorably with the statistics reported from other clinics. However, the percentage survival among patients with cancer of the stump is lower than it is in all patients with cervix cancer treated at Memorial Hospital. Comparison of the five-year results obtained in the treated patients of the two groups illustrates the difference. Among the patients with early disease 43 per cent of those with stump cancer survived, while 50 to 60 per cent of all patients with the same degree of disease involvement have survived for this period of time. In those with advanced disease 7 per cent of the patients with cancer of the stump lived for five years, as opposed to from 10 per cent to 15 per cent of all cervix cases. The total five-year salvage shows the same discrepancy. Only 14 per cent of the 36 patients with stump cancer treated before 1929 lived for five years, as compared with 20 to 24 per cent of all cervix cases.

The poor results obtained in patients with carcinoma of the cervical stump may be partially explained by the anatomical difficulties encountered in making a correct application of radium. The usual tandem employed in the treatment of cervix cancer cannot be used because of the absence of the uterine corpus. In most patients with stump cancer a single capsule can be placed in the canal of the remaining vaginal

portion of the cervix. However, in many patients the cervix has been partially destroyed by the disease, and the radium can only be packed into an ulcerated crater. In the latter instance the radium is frequently left in place for a lesser dose than would ordinarily be used, in order to protect the bladder and rectum from an excessive amount of radiation. Also, a lesser tissue dose is obtained because of the poorer distribution of radiation from such a faulty application. This of course results in inadequate treatment for these patients. It should again be mentioned that radium applied to the cervix is capable of controlling the disease only in and directly adjacent to the cervix. External irradiation must be relied upon for adequate treatment of malignant disease beyond this region. The absence of the uterine corpus should not interfere with the use of roentgen radiation, which may also be used to supplement the treatment of the primary lesion.

Another possible explanation of the poor results obtained in patients with stump cancer is the fact that the carcinoma is located in scar tissue resulting from the previous hysterectomy. The tumor may be accustomed to a poor blood supply before treatment is begun. In such a condition the radiosensitivity of the lesion would be affected, because the sclerosis of blood vessels is an important factor in the causation of tumor regression by radiation.

Whether the presence or absence of ovaries influences the response of the tumor to radiation is unknown. There were 16 patients in the series who were known to have had both ovaries removed. These patients were distributed throughout all the age groups. Seven were classified as having a favorable prognosis and 9 had advanced disease. The yearly survival of these patients was not found to be different from their respective groups, nor was the combined salvage rate different from that of all stump cases.

In an analysis of the treatment given to patients with carcinoma of the cervical stump, it is necessary to consider the dose delivered to each individual.* For a comparison some unit representing an amount of radiation must be employed. The so-called "threshold erythema" serves very well for this purpose. This has been defined by Quimby¹² as representing an amount of radiation which will produce a visible reddening of the skin in 80 per cent of the individuals receiving the exposure, and no visible reaction in the remaining 20 per cent. While the definition originally related to external irradiation by x-rays or radium, it has been extended by Quimby and Martin¹³ to interpret dosages from interstitial sources of radium, such as seeds, needles, tandems, etc.

The dose obtained in the cervix has been chosen for the comparison of the treatment given to the different patients, because it represents

*Tissue doses have been calculated by Mrs. Edith H. Quimby of the Department of Biophysics, of Memorial Hospital.

the primary lesion. Also, it is in the cervix that the results of irradiation can be visually appreciated. The changes in the primary lesion are important for estimating the clinical result, especially as regards the healing of the cervix, or so-called "primary cure." In calculating the dose each patient received, the amount of radiation delivered to the primary lesion by the use of radium locally and by external irradiation has been considered.

In most patients the bulk of the cervix can be included in a sphere 3 cm. in diameter. This volume would also approximate the average size of the primary lesion among those patients in whom the portio vaginalis had not been destroyed by the tumor process. For each patient, the tissue dose was calculated in terms of threshold erythemas for a point on the periphery of the sphere. This point was 1.5 cm. lateral to the canal at a depth of 1.5 cm. in the cervix. The deter-

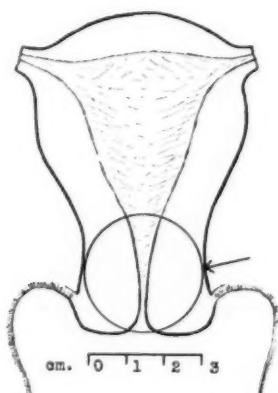


Fig. 1.—Diagrammatic illustration of the point chosen for the calculation of the minimum tissue dose delivered to the primary lesion.

mined dose then represented the minimum quantity of radiation delivered to any point within this volume. In other words, this would be an approximate value of the minimum tissue dose delivered within the primary lesion.

For individuals in whom the malignant disease had eroded a crater, or destroyed the cervix, the procedure was not so simple. In calculating the dose these patients received, a sphere 3 cm. in diameter could not be considered as representing the size of the primary lesion. It was necessary, therefore, to determine its size and the volume throughout which the radium was distributed, as accurately as possible from the description contained in the patient's clinical record. The dose delivered to the primary lesion could then be calculated on a comparable basis with the other patients. The estimation of tissue doses under any circumstance is only approximate, but such a procedure does offer an excellent measure for the comparison of treatment in different individuals.

In both the favorable and unfavorable groups the patients were divided into subgroups according to the tissue dose that had been delivered to the primary lesion. The yearly survival for each subdivision was then determined, depending upon the percentage of living patients among those who had come under observation for the specified number of years. For instance, a patient first observed in 1930, or three years ago, would appear under the first, second, and third years, but not under the fourth. Because of the small number of patients in each subgroup the percentage survival has been converted into the nearest number divisible by five.

In the patients with a favorable prognosis the malignant disease was largely confined to the cervical region, as far as could be determined from clinical examination. A good result could, therefore, be expected in most cases from the application of radium to the cervix alone, provided a lethal tumor dose was delivered. The minimum dose any of these patients received in the primary lesion was from 4 to 6 threshold erythemas. The small number of patients in each of the subgroups representing various doses of radiation does not justify any definite conclusion upon the effect of different amounts of treatment. However, the fact that a primary cure was obtained in every patient except one in the group that received a minimum dose of 6 to 8 threshold erythemas, and the fact that in no case did disease reappear in the cervix after a primary cure had been obtained, indicates that adequate treatment was given to the cervical region in most instances in this group.

All of these patients lived for at least two years after treatment. This excellent result may be attributed to the early stage of the disease, and the relatively high minimum dose delivered to the primary lesion. It seems logical to assume that the loss of patients after the second and third years following treatment may be attributed to uncontrolled disease located at a distance beyond the range of radium applied to the local lesion. There were only 3 patients who received as much as 2 threshold erythema doses in the parametrial regions. This dose was obtained by roentgen irradiation, and has no relation to the tissue dose discussed for the primary lesions. Two of these patients were treated only a year ago, but the third is living and free of disease four years after treatment. This isolated patient tends to illustrate that a better salvage might be expected if this method of treatment were employed more vigorously.

In the analysis of the advanced cases 6 patients have not been included. Three of these received no treatment because of their hopeless prognosis, as has been stated before. Two were not included because they failed to return for the completion of their treatment. One patient has been treated too recently to warrant any comment upon the result obtained. However, analysis of the remaining 43

TABLE II. CLASSIFICATION OF THE 18 FAVORABLE CASES ACCORDING TO THE AMOUNT OF RADIATION DELIVERED TO THE PRIMARY LESION

THRESH- OLD ERYTH- EMA DOSES		YEARS SINCE TREATMENT										PRI- MARY CURE	RE- NEWED ACTIVITY IN CERVIX
		1	2	3	4	5	6	7	8	9	10		
4 to 6	Number of patients	5*	3	2								(5)	(0)
	Per cent survival	100	100	50								100%	
6 to 8	Number of patients	4*	3	3	2	2	2	2	2			(3)	(0)
	Per cent survival	100	100	100	50	50	50	50	50			75%	
8 to 12	Number of patients	9	9	8	7*	5	4	2	2	2	1	(9)	(0)
	Per cent survival	100	100	85	55	40	25	-	-	-	-	100%	

*Indicates a patient who received as much as 2 threshold erythema doses in the parametrial regions from external irradiation.

patients with advanced disease has proved more instructive than the study of the favorable cases, because of the wider variation in the amount of radiation they received, and the larger number of patients in each treatment group.

The yearly survival rate increased with the amount of treatment delivered to the primary lesion. Among the patients who received a minimum dose of 1 to 4 threshold erythemas, only 75 per cent survived the first year. If a minimum tissue dose of 4 to 6 threshold erythemas was delivered to the primary lesion, 85 per cent lived for that time, and with greater amounts of treatment from 90 per cent to 100 per cent survived one year. In the same order the four-year salvage increased from 15 per cent of those who received the smallest amount of radiation four or more years ago, to 30 per cent or 40 per cent if they received a minimum dose of more than 6 threshold erythemas. None of the patients treated five or more years ago who received less than 6 threshold erythema doses in the primary lesion lived longer than four years. However, among those with a tissue dose of 6 to 8 threshold erythemas, one patient lived for five years, and another in the group that received 8 to 12 threshold erythema doses is still living and free of disease for the same period of time. These 2 patients among the 12 who received a minimum tissue dose of 6 threshold erythemas at least five years ago, represent a five-year salvage of 15 per cent. This result is comparable to that obtained in all patients with cervix cancer with advanced disease.

Definitely improved results with heavier treatment can also be illustrated by the number of primary cures that were obtained in the

advanced group. This result occurred in only 35 to 50 per cent of the patients who received less than 6 threshold erythemas as the minimum dose within the primary lesion, but in 75 per cent if more than that amount of radiation was delivered.

The reappearance of malignant disease in the cervix after a primary cure has resulted may be interpreted as evidence that the primary lesion has been insufficiently irradiated. Of the 3 patients who attained a primary cure in the group that received from 1 to 4 threshold erythema doses, there were 2 who developed renewed activity in the cervix. The incidence of such reappearances was reduced to 15 per cent among those who received 4 to 6 threshold erythema doses, and to 10 per cent in those with a tissue dose of 6 to 8 threshold erythemas. None of the patients who received 8 to 12 threshold erythema doses showed activity in the cervix after a primary cure had been obtained.

There were 7 patients among the advanced cases who received 2 threshold erythema doses in the parametrial regions from external irradiation. One of this number was in the group that received a tissue dose of 1 to 4 threshold erythemas in the primary lesion. This patient lived for four years. Two others were among those who received 4 to 6 threshold erythema doses, and survived for two and four years, respectively. There were also 2 in the group that received 6 to 8 threshold erythema doses, both of whom are living for one and

TABLE III. CLASSIFICATION OF 43 ADVANCED CASES ACCORDING TO THE AMOUNT OF RADIATION THEY RECEIVED IN THE PRIMARY LESION

THRESH- OLD ERYTH- EMA DOSES		YEARS SINCE TREATMENT										PRI- MARY CURE	RE- NEWED ACTIVITY IN CERVIX
		1	2	3	4	5	6	7	8	9	10		
1 to 4	Number of patients	9	8	7	7*	7	7	5	5	5	3	(3)	(2)
	Per cent survival	75	50	45	15	-	-	-	-	-	-	35%	65%
4 to 6	Number of patients	12	11*	10	10*	8	8	7	7	5	5	(6)	(1)
	Per cent survival	85	75	30	10	-	-	-	-	-	-	50%	15%
6 to 8	Number of patients	13*	11*	8	7	6	5	5	3	3	2	(10)	(1)
	Per cent survival	100	75	40	30	15	-	-	-	-	-	75%	10%
8 to 12	Number of patients	8	8	8	8	6	4	3	1			(6)	(0)
	Per cent survival	90	75	40	40	15	-	-	-			75%	

*Indicates a patient who received as much as two threshold erythema doses in the parametrial regions from external irradiation.

two years after treatment. The remaining 2 patients who received this amount of external irradiation were among those with a tissue dose of 8 to 12 threshold erythemas. One of these lived for four years after treatment, and the other is still living and free of disease for the same period of time. It is interesting to note, that 4 of the 7 patients who survived a span of four years after treatment, had received 2 threshold erythema doses in the parametria at about the same time that the radium treatment was given to the primary lesion.

From this study of the yearly salvage in patients with advanced stump carcinoma and of the changes occurring in the primary lesion, such as the percentage of primary cures and the incidence of renewed activity of the disease in the cervix, it is apparent that the best results were obtained in the groups that received the two greater amounts of treatment. The percentage of primary cures among the patients who received a minimum dose of 8 to 12 threshold erythemas was not greater than it was in the group that received 6 to 8 threshold erythema doses. In both of these groups the five-year salvage compared favorably with the results obtained in all patients with advanced carcinoma of the cervix. Therefore, a minimum of 6 to 8 threshold erythema doses delivered throughout the primary lesion probably represents the minimum amount of radiation required for a lethal dose to cervix cancer, when administered at the rate, and by the method used in the treatment of these patients. If the primary lesion requires this dosage, control of parametrial disease no doubt necessitates at least the same amount of radiation. It must be remembered that most of the treatment given to the local lesion in these patients was by radium applied to the cervix. The strength of the radium capsules was sufficiently great to deliver the required dose in about twenty-four hours. Radiation was, therefore, administered at a relatively high intensity. None of the patients received more than 2 threshold erythema doses in the parametrial regions, delivered by two courses of roentgen ray treatment with at least a six-week interval between the two cycles. To deliver 6 to 8 threshold erythema doses to the parametrial disease by external irradiation would necessitate a protracted treatment with multiple small exposures. It is doubtful that 6 to 8 threshold erythema doses delivered at a slow rate of administration would have as marked a biologic effect upon the tumor as the same dose delivered over a short time. Further investigations in the technic and methods of roentgen ray treatment may result in a greater salvage of patients with carcinoma of the cervix, than is attained at the present time.

Complete treatment by the method employed at Memorial Hospital requires about eight weeks. For the past few years the routine treatment for carcinoma of the cervix has consisted of a high voltage pelvic cycle of single exposures delivering 700 roentgens to each of four

pelvic fields. About seven to ten days after the roentgen ray treatment has been completed, a vaginal applicator containing radon is placed against the primary lesion for a dose of 1,500 mc. hours, and an intracervical tandem for 3,000 mc. hours. Six weeks after the radium treatment the roentgen ray cycle has been repeated. By this method the average patient receives a minimum dose of about 7 to 8 threshold erythemas in the primary lesion, and about 2 threshold erythema doses in the parametrial regions. The wide variation in the tissue doses recorded for the primary lesion in the different patients of this series has been due to the difficulties of making a correct application of radium within the cervical canal of some patients.

In order to increase the parametrial dose we have begun a plan of multiple exposures to each of the pelvic fields for a protracted roentgen ray treatment at a different rate of administration.¹⁴ By this means from 4 to 5 threshold erythema doses may be delivered to the bulk of the parametrial regions within a period of three or four weeks. The primary lesion receives about 5 threshold erythema doses from the external irradiation alone. This treatment has been followed by the usual radium applications with encouraging results. By carefully planning the treatment of patients with stump cancer a tissue dose may be obtained that is comparable to the amount of radiation which has been delivered to all other patients with cervix cancers. If adequate treatment is given the total salvage of patients with stump cancer should be raised to equal that of all patients with carcinoma of the cervix.

The constitutional effect upon the patient is important in the consideration of different amounts of treatment. Among the advanced cases in which treatment was completed there were 4 patients who developed fistulas. Three of these were of the vesicovaginal type, and occurred in patients who had received a minimum dose of less than 6 threshold erythemas in the primary lesion. Careful examination of the clinical records of these three patients indicated that the fistulas had resulted from extension of uncontrolled disease. The fourth patient was in the group that received 8 to 12 threshold erythema doses. When the treatment was given, disease was present in the rectovaginal septum where the fistulous tract later developed. The heavy irradiation possibly precipitated the development of the fistula, but disease was so advanced that the patient did not survive the first year. The occurrence of vesicovaginal or rectovaginal fistulas does not seem to be related to overirradiation, as much as it does to the presence or extension of uncontrolled disease.

Dean¹⁵ states that bladder injuries following irradiation for uterine disease usually appear several years after treatment. He found that 2.1 per cent of patients irradiated for cervical carcinoma at the Me-

morial Hospital developed bladder sequelae. There has been only one of the treated patients in this series of stump cancers who has suffered any bladder injury, other than the development of fistulas as already mentioned. This patient had an advanced lesion and was in the group that received a minimum dose of 6 to 8 threshold erythemas in the primary lesion. This amount of radiation probably represents the upper margin of safety to normal tissues, when administered at the intensity, and over the time that these patients have been treated.

SUMMARY AND CONCLUSIONS

A series of 67 patients with carcinoma of the cervical stump were studied. There was reasonable evidence that in every patient the disease developed after supracervical hysterectomy had been performed. The low incidence of stump carcinoma does not justify risking the increased mortality of total hysterectomy instead of the subtotal operation, to prevent the later occurrence of cervix cancer in all patients from whom the uterine corpus is to be removed.

The patients were comparable in age, clinical extent of disease, histologic grouping, and symptomatology with all cases of cervix carcinoma. The five-year salvage of patients with stump cancer treated at least five years ago was 14 per cent, which is lower than the percentage survival of all patients with carcinoma of the cervix. The poor results may be attributed to insufficient irradiation, partially due to the difficulties encountered in making a correct application of radium in the absence of the uterine corpus. In most patients a single capsule of radium could be placed in the canal of the remaining cervix. However, in many cases the cervix had been destroyed by the disease, leaving an ulcerated crater in the vaginal vault. In the latter instance it was necessary to pack the radium against the lesion, which is less advantageous for treatment because of the poorer distribution of radiation resulting from such a faulty application. From an analysis of the treatment given the different patients, we may conclude that control of the primary lesion requires a minimum dose distribution of at least 6 to 8 threshold erythemas, when administered in the manner described. The five-year salvage of the patients with advanced disease who did receive this amount of radiation or more, as the minimum dose in the primary lesion, was 15 per cent. This result is comparable to that obtained in all patients with advanced cervix carcinoma in whom the uterus has not been removed for some preexisting surgical condition. If the primary lesion requires this dose, control of the parametrial disease, no doubt, necessitates at least an equal amount of radiation, which cannot be delivered by radium applied only to the cervix. The benefit obtained from only 2 threshold erythema doses delivered by external irradiation to the parametrial regions has been demonstrated.

By administering external radiation in small doses over a longer period of time, a greater total dose can be delivered to the parametria, than has been obtained in the past. Such a method, employing a different rate of administration than has been used in the treatment of stump carcinoma, may prove more effective in controlling the malignant disease in these regions. External irradiation can also be used to supplement the dose delivered to the primary lesion. By this means the inadequate treatment given to the cervix, because of the anatomical difficulties in making a satisfactory application of radium in some cases, may be overcome.

Patients who had already undergone a major surgical operation might be expected to report to their physician more promptly after the onset of unusual symptoms, than those who have had no previous illness. It is interesting to note that the patients in this series did not apply for medical aid any sooner than other cases of cervix carcinoma. The importance of medical education of the public cannot be overestimated in the control of cancer.

The authors wish to express their indebtedness to Mrs. Edith H. Quimby of the Department of Biophysics, without whose assistance it would have been impossible to carry on this work.

REFERENCES

- (1) Chrobak, R.: *Monatschr. f. Geburtsh. u. Gynäk.* 3: 177, 1896. (2) Condamin, R.: *Semaine Gynécologique* 7: 113, 1902. (3) Gilbert, W. H.: *California & West. Med.* 35: 262, 1931. (4) Hochman, S. S.: *AM. J. OBST. & GYNEC.* 11: 566, 1926. (5) Polak, J. O.: *New York State J. Med.* 21: 45, 1921. (6) Healy, W. P.: *AM. J. OBST. & GYNEC.* 26: 789, 1933. (7) Zampa, G.: *Il Policlinico (Sez. Chir.)* 37: 457, 1930. (8) Monod, R.: *Bruxelles-méd.* 10: (2): 1087, 1929-30. Monod, R.: *Gynécologie* 30: 106, 1931. (9) Pinsan, J. R.: *Rev. franç. de gynéc. et d'obstét.* 25: 688, 1930. (10) Polosson, M. E.: *Lyon chir.* 27: 697, 1930. (11) Branscomb, L.: *AM. J. OBST. & GYNEC.* 20: 66, 1930. (12) Quimby, E. H.: *Am. J. Roentgenol.* 17: 621, 1927. (13) Martin, H. E., and Quimby, E. H.: *Am. J. Roentgenol.* 23: 173, 1930. (14) Healy, W. P., and Arneson, A. N.: *Am. J. Roentgenol.* 32: No. 5, 1934. (15) Dean, A. L.: *AM. J. OBST. & GYNEC.* 25: 667, 1933.

Stetten, DeWitt: *Menstruation After Abdominal Operations*, *Am. J. Surg.* 23: 361, 1934.

The author observed that if a woman on whom an abdominal operation has recently been performed begins to menstruate, either at the time that corresponds to her regular period, or especially before her regular period, it is almost a certainty that the postoperative course will be smooth and uneventful. This sign seems to be so consistent and is so nearly infallible, that no matter how critically ill the patient may have been, or how serious the operative procedure was, as soon as this sign appears the author is relieved of further anxiety. If the flow appears the day after operation, and particularly if the appearance is before it is normally due, the convalescence will be especially uneventful, although its non-appearance does not necessarily indicate an unfavorable prognosis.

J. THORNWELL WITHERSPOON.

MATERNAL, FETAL, AND NEONATAL MORBIDITY AND MORTALITY*

FRED L. ADAIR, M.D., CHICAGO, ILL.

(Chairman and Professor in the Department of Obstetrics and Gynecology, The University of Chicago, and The Chicago Lying-in Hospital)

IT IS difficult enough to analyze mortality statistics and secure accurate and comparable results. Statistics of morbidity are much more difficult to evaluate because the condition is poorly defined and there are very few comparable standards for different institutions and various communities. If anyone doubts the accuracy of this observation, then let him attempt to secure uniformity of opinion relative to such a simple standard as temperature as an index of febrile morbidity, or endeavor to obtain a generally accepted definition of puerperal infection.

In general, maternal morbidity and mortality statistics are undoubtedly more reliable than those pertaining to the fetus and newborn infant. It should always be remembered that no study of statistical reports can be more accurate than the original source. We all know how far death certificates fall short of absolute accuracy and, of course, all of our mortality statistics are based on death certificates. Naturally, the more careful study of patients before and after death tends to make the final statistical analysis more accurate. If such data are compared with those from other sources where less care is exercised, the results are not exactly comparable.

Furthermore, there are often more causes than one to which deaths may be attributed. In these cases, opinions may differ and rules may vary for the proper assignment of the primary cause. This is particularly true in various countries, not all of which have agreed to follow the same standards and rules. It is for this reason, among others, that there has been so much discussion relative to the exact position which the United States occupies with reference to maternal mortality in the family of nations.

Dr. Elizabeth Tandy has recently completed a report on "Comparability of the Maternal Mortality Rates of the United States and Certain Foreign Countries." The assembling of this material was begun by a Committee of the White House Conference on Child Health and Protection. This report is simply a study of the methods of assignment of maternal deaths as practiced in various countries. It has nothing to do with the study of the actual causes of maternal deaths. Sixteen countries made the assignment of these deaths from data appearing on

*President's address before the Chicago Gynecological Society, June 22, 1934.

the death certificates sent to them. These assignments are believed to be indicative of present conditions and those which existed in 1927.

The mortality rates are not absolutely comparable for the various countries, but the methods of assignment in the United States correspond closely with those of Australia, Netherlands, New Zealand, and Scotland. The method now used in Denmark gives a higher rate, and the procedure employed in the other countries yields a lower rate than that of the United States. If one applies the rules of other countries the rate in the United States is lower, but a relatively high rate still remains which cannot be explained solely by variations in methods of assignment.

In most instances, the methods used in other countries lower our death rates from puerperal causes, but not sufficiently to remove the United States from its position near the top of the list of those having the highest maternal mortality rates.

It is still incumbent upon us to understand the cause for these high rates and to continue our efforts to reduce our casualties.

At first thought maternal and fetal morbidity and mortality would seem to be simply the sum total of the dire results of uncontrollable causes of the type of obstetric care rendered to individual patients. In a sense this is true, but on the other hand it must be recognized that there are great social and medical movements taking place, and over these the individual doctor and patient have relatively little control. Among these might be mentioned many changes which have taken place within the last fifty years and even a shorter lapse of time.

The increase in hospital beds has been enormous, followed by a tremendous increase in the hospitalization of maternity patients. Changed housing conditions have been a factor in bringing this about. There are now enough maternity beds in this country to accommodate practically all women having babies. They are not all ideal, but they exist, even though the institutions are not properly distributed geographically.

There has been much in favor of hospitalization of maternity cases from the points of view of both the patient and the physician. In many instances, the institutions were not properly planned and equipped for the adequate care of these patients. The personnel, both nurses and doctors, have too frequently had insufficient education and training in this field, as a rule through no fault of their own.

There has been much popular and medical propaganda for a quick and easy delivery at the expense of a safe one. This has led to the indiscriminate use of numerous analgesic and anesthetic agents and the frequent injudicious resort to operative procedures.

For many years past, a greater general interest in health problems and maternal and infant welfare, as well as other matters of vast social import, have led to more extensive individual and public interest in morbidity and mortality associated with maternity. There is no doubt

that in most countries health is a matter which is considered to be of increasing importance to both the individual and the community. Undoubtedly, on the one hand, the development of greater humanitarian ideals has been an important factor in producing these human interests. On the other hand, social conditions have arisen which have made the conservation of the health and lives of mothers and infants of greater importance to various states.

BIRTH RATE

Our mode of life and love of comfort and pleasure, together with economic and other social conditions, have generated a desire to limit the size of families, which is clearly shown in our rapidly diminishing birth rate and increasing number of abortions during the present century. Many of these conditions are not peculiar to this country, but are also met in many European countries.

It is estimated that a birth rate of 16.6 per 1,000 persons is necessary to maintain a stationary population. This would necessitate about 3.4 children per family. The statistics relative to the birth rate in the United States prior to 1915, when the registration area was established, are not very accurate. At this time the rate was 25 per 1,000 population. Since 1915, the trend of the birth rate has been steadily downward to 17.3 in 1932. If this decline were projected into 1933 and 1934, the probable rate would be below that which would be required to stabilize the population.

It is obvious that if this decline continues there will be a gradual diminution in the growth of the population, at least in those countries which continue to have a diminishing number of births. If this becomes world-wide, it will mean a gradual reduction in the total population of the world. If the birth rate declines in some countries and some civilizations, and increases in others, it will mean an ultimate shift in national or racial domination. The same logic may be applied to groups within any given country, whether they are social, racial, or otherwise. In other words, within a more or less circumscribed community, the group with the highest birth rate and survival will ultimately dominate. Therefore, it becomes of great importance to races, nations, and various groups within nations to conserve the reproductive assets of the more desirable individuals. No one can determine which is the most desirable group or who the ultimate survivors will be. Various factors are responsible for the reduction in the birth rate, and it behooves us to consider the desirability of using some of these agencies to curtail the reproduction of individuals who are manifestly undesirable in any community.

The principal factor in the reduction of the birth rate is the rather general desire on the part of individuals to reduce the size of their families in order to cope more successfully with existing social and

economic conditions. This has been accomplished by various measures, such as contraception, sterilization, and abortions, which have steadily increased in number. It is impossible to know to what extent abortions have increased, but various authorities have estimated the number to be from one to every live birth to one of every two or three pregnancies.

It is not at all improbable that there are at least from 750,000 to 1,000,000 abortions in the United States each year. It is certain that maternal deaths from intentional abortions have tended to neutralize the decreased number of maternal deaths which have resulted from improved obstetric practice. It is apparent, therefore, that the desire to limit the size of families, even by measures so radical as the induction of abortion, leads not only to a diminishing birth rate, but also to an increased mortality rate, at least from this cause. The fetus, of course, is a total loss in these cases.

One result of the diminishing birth rate, causing a reduction in the size of families, is that a relatively greater number of women of low parity are delivered each year. In Chicago, during 1933, among 46,655 deliveries, the distribution of parity was as follows: Para i, 40.5 per cent; para ii, 26.9 per cent; and para iii, 14.2 per cent, making a total of over 80 per cent of all deliveries in the city among women with a parity of three or less. Approximately one-half of these women were delivered of their first child. There has been a percentage increase for first children born in the registration area. It was 27.3 per cent of the total number of births in 1917, and 31.9 per cent in 1931.

GENERAL CONSIDERATIONS

It is much easier to define mortality and obtain and analyze statistics pertaining to it than it is to define morbidity and secure accurate statistical analyses concerning it. As a rule, the same conditions and factors which in some cases produce morbidity may in other instances cause mortality. Morbidity may be defined as any condition which departs sufficiently from the normal to produce disability, no matter whether it is immediate or remote, temporary or permanent. Naturally, the degree of disability varies enormously, not only in its intensity but also in its duration. Without morbidity there would be no mortality.

The factors producing morbidity may or may not result in mortality. A fatality may occur close on the heels of the morbid condition, for example, in patients with acute hemorrhages, or death may result after a lapse of days as, for instance, in patients with infection or toxemia. The mortality may be a remote consequence of the primary condition and may occur years after the onset of the morbid state. Such a situation may present itself in vascular or renal diseases which were primarily associated with pregnancy.

Similar conditions exist with reference to the fetus and neonatal infant. Death may occur suddenly from an abnormal condition which causes a very transient morbidity, as in cases of abruptio placentae or prolapsus funis. A traumatic morbid state, as intracranial injury, may lead to rapid death, or the fetus may be born alive with more or less permanent damage, leading eventually to a long-continued disability and terminating ultimately in death.

A congenital condition may be present at birth and may result in a transient or long-continued morbidity and ultimately lead to death of the infant. A fetus may be born alive, apparently healthy, harboring a syphilitic infection which may lead to a protracted course of congenital syphilis, with ultimate handicapped survival or death. An infection, such as ophthalmia neonatorum, may develop in the newborn infant, producing a morbid state from which it may recover completely, or suffer partial or total blindness. An infection of the umbilicus may manifest itself subsequent to birth. This may be of minor consequence or of sufficient seriousness to cause a fatality.

There have been many improvements in maternity care and individual physicians and some institutions show very low morbidity and mortality rates. These good results have been counterbalanced by other factors which tend to and do actually neutralize the good results obtained in some areas.

It is well known that our negro population maintains a constantly high rate for both fetal and maternal morbidity and mortality. It should be clearly recognized that our hospitalization and coexistent operative incidence is unusually high and probably unequalled in any other country in the world.

OBSTETRIC MORTALITY AND MORBIDITY

Both the fetal morbidity and mortality are higher among women of lower parity, which is to say that the risk is greater in the first pregnancies than in subsequent ones, etc.

These are factors of great importance in maintaining obstetric mortality. A rather constant contributory factor is the more general and increasing use of various anesthetic agents, which tend to interfere with normal processes and facilitate, as well as necessitate, a greater incidence of operative deliveries. Another factor is the increased hospitalization of maternity patients, which adds to the safety and facility of operative obstetric procedures. No doubt, the marked increase in hospitalization of patients has resulted in an immoderate number of cesarean sections, which is an example of the increased major surgical intervention in obstetric cases. This statement also applies to increases in the number of other operations of lesser magnitude.

Whether or not the percentage of infections is increased by the hospitalization of patients is, to my mind, not a question of hospitalization or nonhospitalization, but one of the type of hospital into which maternity patients are brought and of the kind of obstetric care which is received.

Reference has already been made to the birth rates and maternal mortality rates. It may be of interest to cite the changes in the death rates over a period of years. The maternal mortality rate per 10,000 live births in the United States registration area has not been under 61 since 1915. It reached a peak of 92 in 1918, and was 63 in 1932. The urban rate has been consistently higher than the rural rate, and has not been under 64 since 1915, or less than 70 since 1917, with a peak of 96 in 1918, and a rate of 74 in 1932. The rural rate has not been below 55 since 1915. It reached a peak of 87 in 1918 and was 54 in 1932.

In Illinois, the general rate was lowest in 1930 and 1931, with a rate of 55. The peak was reached in 1929, with a rate of 68. The rate for 1932 was 56. There is some difference between the urban and rural rates. The lowest urban rate was 58 in 1931 and 1932, and the highest was 73 in 1929. The lowest rural rate was 40 in 1927, the highest was 57 in 1922 and 1929, while the rate in 1932 was 51.

There is a marked difference in the registration area between the maternal mortality in white and colored races, the latter being much higher. The rate for the colored race in 1915 was 106. The peak was reached in 1918, with a rate of 139, and the rate in 1932 was 98, which was the only year during which the 1915 rate was improved. The rate for the colored population in Illinois is considerably higher than for the white population, the maximum being 138 in 1923, and the minimum 65, which was in 1932.

The trend of infant mortality rates has been downward in the registration area since 1915. In 1932, the rates in Illinois per 1,000 live births were 48 in the state as a whole, 58 in urban communities, and 43 in the rural districts. There has been a gradual improvement in the neonatal mortality rate as shown by a constant decline from 44.4 in 1915, to 33.5 in 1932.

The major causes of maternal deaths may be divided into those which accompany or are incidental to the reproductive processes and those which are accidental to it. The former class of causes are grouped mainly under toxemias and traumatic conditions, no matter whether or not they are the result of spontaneous or operative deliveries, or hemorrhage. Most of the associated or accidental causes of maternal deaths may be grouped under such types of disease as infections of genital or extragenital origin, diseases of the cardiovascular-renal system, and pulmonary disease.

The major causes of fatality among the fetuses and the neonatal infants may be divided into those which affect the fetus and those which

destroy the newborn infant. The fetal period may be considered to extend through intrauterine life prior to labor, during parturition, and throughout the period following birth prior to the establishment of respiration, which is the real criterion for the termination of fetal life and the commencement of extrauterine life.

One may feel fully justified in classifying fetal deaths into (1) antenatal, including all fetal fatalities occurring during pregnancy prior to the onset of labor; (2) intranatal, consisting of all casualties during the process of labor, and (3) postnatal, taking place during the period intervening between the birth of the fetus and the establishment of its respiration.

Neonatal deaths are those which occur during the period following the establishment of respiration at birth and the end of the period during which the infant gradually adjusts itself to extrauterine life. This ordinarily requires about two weeks' time. Most of these fatalities are related to obstetric care. The majority of diseases and deaths of infants occurring later are not directly related to maternal care.

The causes of fetal and neonatal morbidity and mortality may be either of maternal, fetal, or extrauterine origin. The former includes all those morbid states which arise in the mother but affect the fetus. All conditions which arise from the germ cells and affect the fetus or fetal adnexa are to be considered as fetal in origin. It is recognized, however, that hereditary factors play a rôle in some of these conditions. In many others fetal and neonatal disorders result from faulty intrauterine or extrauterine environment.

It is difficult in many instances to make a clear-cut distinction between maternal and fetal causes. Hereditary and congenital conditions are responsible for many fetal and some neonatal deaths. Our present knowledge is not sufficient to prevent a development of these conditions. Many previable infants are born as the result of some maternal condition which leads either to intentional or unintentional premature labor. Careful prenatal care will prevent some of these previable and premature terminations of pregnancy.

Such infant fatalities may fit into any one of the varying classifications mentioned above. Our statistics include many deaths of previable infants because it is required that births be reported after a period of five months' gestation. The fetus, of course, does not attain viability until approximately the twenty-eighth week of gestation. Prematurity is an important cause of fetal and infant deaths, but our statistics include among premature infants many which should be classified as previable. The fatalities among premature infants are many because they are particularly susceptible to the etiologic factors which are responsible for the deaths of many infants born at term.

In addition to the general factors already mentioned as causing fetal and neonatal casualties, there are many specific causes for infant deaths

which may be grouped under the following: (1) Trauma affecting various structures and organs, chiefly those of the central nervous system; (2) infections, both acute and chronic, specific or nonspecific; (3) hemorrhages, traumatic or nontraumatic; (4) thermic causes, as refrigeration and insolation; and (5) faulty nutrition, etc.

Practically all of these causes mentioned as productive of mortality are also responsible for fetal and infant morbidity. We know very little relative to fetal morbidity during the antenatal period, although we have acquired some knowledge from the study of conditions which are carried over from this period into subsequent life, especially when fatalities occur. We know much concerning the morbidity of the intranatal period, and more concerning the neonatal period, although, on the whole, there are many gaps in our knowledge covering these special periods of life.

The morbidity may not manifest itself objectively or subjectively during the period when it is primarily acquired. The subsequent course of events reveals the morbid state which may be such as to eventuate in early death, or it may be carried along in an infant or child who is handicapped for a shorter or longer period of his life.

The prevention of the morbidity and mortality of mothers and infants cannot be absolute. The prophylaxis depends upon adequate care for the fetus and the mother, and for the infant from birth onward, which includes preconceptional, antepartum (antenatal), intrapartum (intranatal), postpartum (postnatal), gynecologic, and neonatal and infant care. Such care implies a properly educated laity who will seek and accept such attention, and personnel who are not only educated but also trained and experienced in administering it. Institutions and organizations are required and they must furnish the material, methods and personnel by which maternal and infant care can be supplied to all members of the community who require it.

It is undoubtedly unnecessary to point out that many individual physicians, nurses, etc., can furnish proper care to their own patients. It is, however, important to stress the fact that in many communities such work is not organized in a manner so that all mothers and babies can receive the requisite care either in their own homes or in the hospitals. The physicians of various communities can accomplish much if they will lead in organizing the resources of their own communities, so that adequate care will be available to all mothers and infants in their own localities.

With these general remarks, one may proceed to a consideration of the more specific causes of maternal, fetal, and infant morbidity and mortality.

Our statistics usually do not give a true picture of the course of events. In most cases, death is assigned more or less accurately to some

single cause. In many, and probably most, instances there are combined causes and with propriety the major one is charged with the result.

It is not desirable to fill your minds with statistics, but some presentation of information will give a rather definite idea of the relative importance of some of the many factors which contribute to these maternal and fetal casualties.

Statistics from various sources show that certain causes operate more or less uniformly and in about the same percentage and relative frequency in causing morbidity and mortality of mothers and their progeny. Some statistical facts stand out clearly in a recent report of the maternal mortality study conducted by the Children's Bureau. There were 7,380 maternal deaths analyzed. Over 1,550 of these women had not reached the seventh month, and one-third had not passed the third month of gestation at the time of death.

Some pertinent facts may be gleaned from this report. The mortality rate for colored women was nearly twice that for white women. About 9 per cent of these women had no medical care or received it only when moribund. Over 4,000 of these deaths occurred in hospitals, but the pregnancy was terminated in a hospital in only 2,600 of these cases. Relatively few of these patients had planned hospitalization. About 900 of these women who died during the last trimester had contemplated hospital deliveries. Seven per cent of these deaths occurred in unmarried women.

Over 5,600 of these women might have received prenatal care, but 54 per cent had no prenatal medical examination or care. Less than 1 per cent received adequate prenatal care. Only 13 per cent had good prenatal care, and over 75 per cent had poor, indifferent, or no prenatal attention.

The delivery care was often inadequate; emergency hospitalization was done in over one-half of the patients dying during the last trimester. Eighty-three per cent of these women were delivered by physicians, internes, or medical students, and 11 per cent by midwives. The doctors evaluated their own technic in this study and it was admittedly faulty in more than 50 per cent of the cases. It is interesting to note that more than one-half of these women had some operative procedure. In 37 per cent the operation was for delivery. Of those women who reached the last trimester, 45 per cent had attempted or completed operative deliveries. Details will not be given here, relative to the incidence of the various operative procedures, except to note that cesarean section was performed in 11 per cent of the women who reached the last trimester, and concerning whom information relative to operative procedure is available. Twenty-four per cent of all the operations for delivery were cesarean sections. Toxic states were the most frequent

indications for this operation. The most frequent causes of death in this group were puerperal albuminuria and convulsions, septicemia, and accidents of labor.

Abortions were defined for this report as previable terminations of pregnancy. Seventy-three per cent of the deaths following abortion were from septicemia and constituted 45 per cent of the total deaths from puerperal septicemia.

Puerperal septicemia was the most frequent cause of death and it accounted for 40 per cent of 7,380 deaths. In this series, 1,529 women died from sepsis in the last trimester and, of these, 94 per cent had a spontaneous onset and 65 per cent a spontaneous termination of labor. In 30 per cent of these women, toxemia was the chief or principal contributory cause of death. Twenty-six per cent of these deaths were due to puerperal albuminuria and convulsions. Only 12 per cent of these women had received good prenatal care, and over one-third of them were not seen by a physician prior to death, or were already in convulsions or coma when first seen. Hemorrhage caused 11 per cent of these deaths. Placenta previa, ablatio placentae, postpartum hemorrhage, and other puerperal hemorrhages are all listed. Traumatic conditions, as rupture of the uterus, inversion, etc., make up a small percentage of the total fatalities considered in this study.

There was no special study of fetal and neonatal deaths in connection with this analysis, but incidental data reveal that only 43 per cent of these women gave birth to living children, 8 per cent died undelivered, 29 per cent gave birth to nonviable fetuses, and 20 per cent were delivered of stillborn infants.

Munro Kerr has recently published a treatise dealing with maternal mortality and morbidity and the problems confronting medical practitioners in Great Britain. He recognizes, as do others in various countries, that the maternal mortality rate has remained stationary for years, and that the same etiologic factors continue year after year without material alteration, in spite of the fact that rates from other causes of mortality have been reduced. It is also believed the main reason for this failure to reduce mortality is not the lack of knowledge of measures to prevent these deaths, but neglect of application of known facts. This is evidenced by the observations that mortality is reduced materially where these well-known principles are practiced.

Statistics have been compiled for decennial periods, 1855 to 1930, for England, Wales, and Scotland. The maternal mortality rates for puerperal fever and other puerperal causes show no decrease in the last seventy-five years. It is interesting to note that the causes of mortality have the same order of incidence as was found in our country, viz., puerperal sepsis, eclampsia, hemorrhage, and other diseases and accidents of childbirth.

The percentage of frequency is not markedly different for the two countries, as Kerr gives approximately the following proportions for the causes just mentioned: Sepsis, 38 per cent; toxemias, 18 per cent; and hemorrhages, 12 to 15 per cent.

The outstanding causes of mortality are those mentioned above. Hemorrhage is not a great factor in the causation of resultant disability, the major causes of which are toxemia, infection, and trauma.

It is a curious fact that obstetric mortality has remained fairly constant not only for mothers but also for fetuses and neonatal infants. This is all the more striking when one realizes that other causes of death in women of the childbearing period have been markedly reduced, and that the later infant mortality rate is much less than it was thirty years ago.

The fetal death rate and the neonatal mortality rate have remained about the same for several decades in Great Britain. It is roughly estimated by these authors that congenital conditions cause some of the neonatal deaths, but that birth injury, infection and prematurity are each responsible for approximately 30 per cent of the neonatal deaths. They estimate the fetal death rate at about 185 per 1,000 conceptions.

The statistics from other sources show the same general trends, and it is unnecessary to repeat corroboratory evidence. It is important to call attention to the occurrence of deaths from conditions associated with pregnancy. The pregnancy often seriously complicates and aggravates these conditions, and if the mother does not die during pregnancy or soon after labor, her health may be impaired and her life shortened by a pregnancy complicating a condition in which cardiac, renal, or other vital function is seriously compromised.

One cannot take too myopic a view of maternal lives. It is hardly consistent to spare a life temporarily in the face of a pregnancy complicating a progressive condition which is made definitely worse by permitting the gestation to continue. Nor does it seem reasonable to expose a woman to the risks of repeated pregnancies in the face of a serious chronic or recurring disease.

There is evidence pointing to the conclusion that the first pregnancy is the most dangerous for the mother and the infant, the second and third are less hazardous, but that the fourth and subsequent pregnancies seem to become progressively more dangerous.

The causes of death and disability are quite well known. It is impossible to eliminate all maternal, fetal, and neonatal deaths. We know enough to prevent many of these fatalities. It is not so much the lack of knowledge as the failure to apply it generally which is responsible for the persistently high maternal and fetal morbidity and mortality rates.

THE SYNTHESIS AND EXCRETION OF HIPPURIC ACID IN PREGNANCY

A. HIRSHEIMER, M.D., CLEVELAND, OHIO

(From the Maternity Service, Methodist Episcopal Hospital, Brooklyn, N. Y.)

THE present study was begun because it seemed that the metabolism of benzoic acid in the pregnant woman might be significant in relation to several physiologic functions which may be disturbed in the presence of a fetus and which have hitherto received inadequate attention.

Hippuric acid is present in normal human urine in varying small amounts as the end-product of the detoxification of benzoic acid and benzoates derived from foodstuffs and the splitting of aromatic compounds in the intestine. The conjugation of benzoic acid with glycine to form hippuric acid is typical of the mechanism by which the body takes care of a certain group of related toxins. In man it is felt certain that the conjugation occurs in the kidneys and liver and perhaps other tissues. If it be assumed that the tissues are capable of the synthesis, then the formation of hippuric acid from a given quantity of benzoic acid depends upon the availability of an equivalent quantity of glycine. Since there is but a small amount of the latter circulating and free in the tissues,¹ it, in turn, must be synthesized if much is demanded and none ingested. It seems definite that this synthesis occurs for the most part in the liver. From this fact Quick² has evolved a test of liver function which consists of the quantitative determination of hippuric acid eliminated after the ingestion of a definite amount of sodium benzoate and the comparison of the findings with the expected rate which is constant in normal individuals. The recovery of hippuric acid has so far been found to be low in catarrhal jaundice, hepatitis, syphilitic cirrhosis, and prolonged obstructive jaundice, but may be normal in Laennec's cirrhosis.

Our knowledge of hepatic pathology as found postmortem in the toxemias of pregnancy is complete enough, yet there has been but inconclusive information elicited concerning the development of the functional disturbances of liver physiology which may be of primary importance. Nearly all available tests of liver function have been tried in cases of normal and toxemic pregnancy. These include the phenoltetrachlorophthalein, bromsulphalein, Widal's hemoclastic crisis, Ehrlich, Schlessinger, Fouchet, van den Bergh, nitrogen partition, and levulose tolerance tests. The results have been reviewed by Stander,³ and by Cross.⁴ There is a general agreement that the findings are

negative in normal cases. The Widal, Ehrlich, Schlessinger, Fouchet, and levulose tolerance tests give unreliable results.

In the toxemias the excretion of the dyes is often delayed, but it is not possible thereby to distinguish between nephritic and eclamptic toxemia. Bilirubinemia as indicated by the van den Bergh reaction when found indicates definite liver damage.

Sullivan, Tew, and Watson⁵ have recently reported a series of 80 cases of both normal and toxemic pregnancy on whom determinations were made of the excretion rate of intravenously administered bilirubin. They reviewed similar tests performed previously by Kaufman, Stroebe, Hofbauer, Soffer, and Watson. In general agreement with these others, they found that during the first half of normal pregnancy liver function by this test is unimpaired, but that in the second half evidence of disturbed function can be demonstrated in at least 30 per cent of the cases. Toxic patients with definite signs of renal insufficiency tend to show less retention of injected bilirubin than those with normal kidney function.

It was indicated that the impairment of liver function occurring in both normal and toxic pregnancies is of a temporary nature, since the bilirubin excretion test tends to return to normal following the termination of pregnancy. This test is the only one thus far tried which gives fairly positive indication of disturbed hepatic function in normal pregnancy.

From the foregoing it is apparent that any new approach to an understanding of liver function in pregnancy is worthy of trial.

METHOD

One hour after a light breakfast, from which fruit is excluded, the patient voids and is then given 5.9 gm. of sodium benzoate (the equivalent of 5 gm. benzoic acid) and half a glass of water. The benzoate is conveniently administered as 30 c.c. of a 19.7 per cent solution to which some peppermint water is added to disguise the taste. No further fluids are allowed until the test is completed. Urine is collected at one-hour intervals for four hours. If the urine is not to be treated in a short time it must be preserved with toluol to prevent hydrolysis of the hippuric acid which readily occurs, especially in alkaline urines. For the determination of the hippuric acid the simplified Method I of Quick² was used in this study. Urines containing show, lochia, or albumin must be acidified with acetic acid, boiled, and filtered before further treatment or the final filtration will be much delayed. Specimens with a volume of more than 100 c.c. are acidified with acetic acid and reduced to about 50 c.c. by boiling or evaporation. One cubic centimeter of concentrated HCl is added to each specimen. If this does not produce a reaction acid to Congo red, a generously sufficient further quantity of acid is supplied. The urine is stirred vigorously until precipitation of the hippuric acid is complete, then is allowed to stand for an hour, whereafter the precipitate is collected by filtration. For the filtration it is most convenient to use a filter flask carrying an ordinary 60° glass funnel with a 25 mm. Hirsh filter plate and 4.25 cm. Whatman No. 2 paper. The hippuric acid is allowed to dry in warm air and weighed to the second decimal place. There is so little variation in the filter papers that one can be used for a counter-balance. The filtrate is measured and the amount of hippuric acid remaining in solution calculated by multiplying the volume in cubic centimeters by 0.0033. This added to the weight of the precipitate gives the total hippuric acid recovered in one hour. In order to have a uniform basis of comparison, the hippuric acid is then represented as benzoic acid by multiplying by 0.68.

The average total normal excretion for four hours has been found to be 3 gm. of benzoic acid, hence the total is divided by 3 to get the percentage of average normal. It is also found that the maximum in one hour, usually the second or third, should be about 0.9 gm. or more. The output varies somewhat in relation to the size (the surface area) of the individual and a 90 per cent recovery is to be considered normal for a small subject. Occasionally a test showing a subnormal total output is interpreted as normal when the output for one hour is found to be 0.9 gm. or more. Such interpolation is made necessary by the possibility of delayed absorption of sodium benzoate, though assimilation is normally rapid.

Another possible explanation of a low recovery of hippuric acid than the failure of synthesis must receive consideration, namely, that the kidneys may be unable to excrete it when it has to be formed. This question is particularly likely to arise in the toxemias of pregnancy with hypertension and albuminuria. Quick² states that hippuric acid behaves like other nitrogenous excretory products and that when there is nitrogen retention it too will be retained. The exact state of the kidney threshold to hippuric acid and its variation in kidney dysfunction remains to be determined. It was first thought that patients showing a subnormal excretion of hippuric acid after sodium benzoate could be checked by giving an equivalent quantity (7.33 gm.) of hippuric acid by mouth after conversion to sodium hippurate. This was tried and found not entirely satisfactory. It has been demonstrated that the absorption of sodium hippurate in the rabbit is much slower than of sodium benzoate⁶ and this is apparently also true for man, since after sodium hippurate by mouth the hourly excretion of the hippuric acid is often irregular and even in normal individuals the total hippuric acid excreted in four hours is often less than after an equivalent amount of sodium benzoate. After some indeterminate checks by the oral administration of sodium hippurate, it was decided that only by giving it intravenously could its excretion be definitely determined. This has been done without ill effect in animals. Swick⁷ has found it is feasible to give intravenously for pyelography 10 to 20 gm. of sodium ortho-iodohippurate in 40 per cent solution. This salt is, of course, closely related to the unsubstituted sodium hippurate. He observed that there was a very sharp curve of excretion, 60 to 66 per cent being recovered in the first hour and 70 to 80 per cent in two hours. After a sterile preparation of sodium hippurate, neutral to phenolphthalein, representing 20 per cent of hippuric acid was tried intravenously on myself and my colleagues without untoward reaction, it was used as a check on some patients. Ten cubic centimeters representing 2 gm. of hippuric acid were given at a time, injecting slowly. Occasionally a transient feeling of warmth and flushing without significant change in the pulse rate appeared at the conclusion of the injection. Urines were first collected at one-half, one, and two hours after the injection. In a short series of normal individuals tested it was found that an average of 64 per cent was excreted in the first half hour, an additional 14 per cent at the end of an hour, and only 8 per cent more after the lapse of the second hour. Hence it is felt that any delay in the first thirty minutes and a low total for one hour represents a diminished renal capacity for the excretion of hippuric acid. Kingsbury and Swanson,⁸ Bryan,⁹ and Morgulis, Pratt, and Jahr¹⁰ have investigated the excretion of hippuric acid as a test of renal function on the premise that the synthesis occurs in the kidney. The conjugation of benzoic acid in man is probably not limited to the kidney. It is likely that the excretory mechanism of the kidney behaves in relation to hippuric acid much as it does to other nitrogenous metabolites. The above investigators gave sodium benzoate by mouth equivalent to 2 gm. of benzoic acid and calculated the percentage of benzoic acid recovered from the urine at two and three hours in the first two investigations, and at six and twenty-four hours in the last. Kingsbury

TABLE I. EXCRETION OF HIPPURIC ACID AFTER SODIUM BENZOATE AND SODIUM HIPPURATE BY MOUTH

CASE	HOSP. NO.	AGE	PARITY	WEIGHT LBS.	GESTA- TION	HOURLY OUTPUT OF HIPPURIC ACID AS GRAMS OF BENZOIC ACID					% NORMAL	REMARKS	TENTATIVE DIAGNOSIS
						1	2	3	4	TOTAL			
1	# 15110	25	i	168	Term + 11	0.2 0.54	0.53 0.81	0.22 1.01	0.91 0.77	1.86 3.13	62 104	? Irregular absorption in 1st test. Nephrectomy 1930 tendency to hypertension with intermittent rise of B.P. At term 140/100 falling to normal postpartum. B. U. N. 12. Uric acid 4.	Low reserve kidney.
2	M. G. (O. P. D.)	28	ii	230	-160	0.40	1.14	1.07	0.48	3.09	103		Normal
3	G. C. (O. P. D.)	22	i	145	-162	0.56	0.68	0.99	0.41	2.64	88		Normal
4	# 15160	18	i	140	- 17 + 10	0.25 0.82	0.61 0.72	0.67 0.84	Lost 0.72	3.10	103	Intermittent hypertension late in pregnancy. At term 150/100. Albuminuria + + 4th specimen lost in 1st test. Test nevertheless subnormal.	Low reserve kidney.
5	# 15118	21	i	130	Term + 11	0.35 0.18	0.50 0.33	0.59 0.43	0.88 0.90	2.32 1.84	77 61	Urine in 2nd test stood without preservative. Hydrolysis likely.	Normal.
6	M. J. (O. P. D.)	32	i	165	- 76	0.22	0.75	0.75	0.54	2.26	75		Normal.
7	# 15125	28	ii	124	- 1 Term* + 10	0.24 1.00 0.71	0.27 0.55 1.37	0.98 0.82 0.62	0.86 0.48 0.45	2.35 2.85 3.15	78 95 105	*7.3 gm. hippuric acid by mouth.	Normal.

Unless otherwise indicated, figures are results after 5.9 gm. sodium benzoate by mouth.

In the sixth column the figures designated minus (-) give the number of days before calculated term or delivery, plus (+) the number of days postpartum.

TABLE I—CONT'D

8	#15099	30	ii	165	+ 11	0.14	0.69	1.57	1.54	3.25	108		Normal.
9	#14648	22	i	143	+ 10	0.25 0.24	0.68 0.97	0.68 0.92	0.74 1.05	2.36 3.18	78 106		Normal.
10	E.H. (O.P.D.)	27	i	117	- 89	0.67	0.84	0.96	0.90	3.37	112		Normal.
11	A.D. (O.P.D.)	26	i	165	- 36	0.48	0.76	0.90	0.81	2.95	98		Normal.
12	#15145	32	ii	139	- 8 - 6* + 11	0.28 0.25 0.79	0.52 1.13 0.22	0.65 0.77 0.89	1.00 0.36 1.03	2.45 2.51 2.93	82 83 98	*7.3 gm. hippuric acid by mouth.	Normal.
13	#15150	23	i	202	- 1 - 2* + 9	1.37 0.42	0.84 1.53	0.93 0.35 1.06	1.34 0.29 0.66	2.27 2.85 3.67	76 95 122	*7.3 gm. hippuric acid by mouth. Hypertension since first seen in 7th month. Albuminuria 1 month. B.P. at term 160/112. Albuminuria + B.U.N. 17. 10 days post-partum B.P. 140/100. 15 minute renal function normal total, low first specimen.	Chronic nephritis.
14	#15156	30	i	163	- 1 + 11	0.14 4 hour specimen	0.60 specimen	0.75	0.55	2.04 2.90	68 97	Normal until term when B.P. rose to 160/94 and albuminuria appeared. B.U.N. 9.4. Uric acid 3.7. B.P. normal on discharge.	Low reserve kidney.

TABLE I—CONT'D

CASE	HOSP. NO.	AGE	PARITY	WEIGHT LBS.	GESTA- TION	HOURLY OUTPUT OF HIPPURIC ACID AS GRAMS OF BENZOIC ACID					% NORMAL	REMARKS	TENTATIVE DIAGNOSIS
						1	2	3	4	TOTAL			
15	#15141	23	ii	130	-184 -178	0.46 0.37	0.45 0.77	0.75 0.67	0.48 0.67	2.14 2.48	71 83	Vomiting 8 weeks. Icteric index 40. B. U. N. 36. Uric acid 9 on admission falling to normal shortly. Icteric index 5 on day of first test.	Hyperemesis gravidarum.
16	R. L. (O. P. D.)	20	i	120	-200	0.18	0.95	0.90	0.86	2.89	96		Normal.
17	#15197	29	ii	165	- 7	0.66	0.96	1.18	0.58	3.38	112	Slight hypertension since 5th month 132/70 to 142/90. At term 148/80. Occasional faint trace of albumin.	Low reserve kidney.
18	#15172	23	i	148	- 8 + 10	0.24 0.67	0.96 0.96	0.71 1.09	0.35 0.82	2.46 3.54	82 115	One transient rise in B. P. to 138/100. No albuminuria.	Low reserve kidney.
19	#15182	31	i		Term	0.14	0.60	0.66	0.40	1.80	60	B. P. 140/90 albumin + last three weeks. B. U. N. 15. Uric acid 4.2.	Low reserve kidney.
20	#15078	34	viii	174	- 6 + 9	0.18 0.59	0.73 0.92		0.43 0.88	1.34 3.46	45 115	Systolic hypertension with faint trace of albumin since first seen in 5th month. B. P. at term 132/90. Stillbirth. Cord and placenta show syphilitic histology. Maternal Wassermann negative.	Chronic nephritis. ? Syphilis

TABLE I—CONT'D

21	#15205	29	i	151	Term + 10	0.41 1.09	0.76 1.77	0.60 1.09	0.82 0.12	2.59 4.07	86 138	Trace albumin 1 week before term, B.P. normal. On admission B.P. 178/98. Albumin +, sl. edema, no symptoms. B.P. labile but returned to normal postpartum.	Pre-eclamptic toxemia.
22	#16333	31	iii	148	+ 2 + 11	0.37 0.60	0.85 1.07	0.29 1.09	0.94 0.77	2.65 3.53	88 114	Previous deliveries and antepartum course normal. Postpartum B.P. 164/100, moderate headache, albumin slightest possible trace. B.U.N. 21. Uric acid 6.3. B.P. fell to normal by fifth day.	Postpartum. Pre-eclamptic toxemia.
23	#15206	22	i	163	- 2 + 10	0.41 0.32	0.72 1.16	0.46 1.22	0.17 Lost	1.76	59	Slight albuminuria without hypertension since 7th month. B.P. postpartum 132/100 falling to normal by tenth day. Fourth specimen lost in second test, but return obviously normal.	Low reserve kidney.
24	#2182A	42	v	160	- 39	0.27	1.37	0.62	0.50	2.76	92	Previous deliveries normal except for occasional slight albuminuria. Hypertension and albuminuria since seventh month. B.P. 140/90 to 168/100.	Chronic nephritis.

and Swanson, and Bryan considered a recovery of 70 per cent in two hours, and 85 to 90 per cent in three hours as normal, and found the recovery diminished in certain cases with kidney dysfunction.

Bryan tested 12 normal pregnant and puerperal women with normal results, 12 cases which were considered abnormal on the basis of a past history of scarlatina, tonsillitis, or rheumatism were found to have diminished two-hour phenolsulphonephthalein tests, averaging 44 per cent and benzoic acid recovery of 49 per cent at the second hour and a total of 76 per cent at the third. One patient had "toxemia," one puerperal fever. No other clinical findings are given. Morgulis, Pratt, and Jahr based part of their interpretation on the recovery of free benzoic acid, and Bryan considered the presence of as much as 3 per cent free benzoic acid as an index of hepatic dysfunction. It is more probable that the free benzoic acid was the result of the hydrolysis of hippuric acid, and perhaps of small quantities of glycuronic acid monobenzoate in standing urine, which readily occurs if the urine is not treated with preservatives or analyzed at once.

Because these workers used both a different quantity of benzoate and a different analytical method, it is not possible to draw a close comparison between their results and those presented herein. I feel, in addition, that the state of renal function in their patients cannot be unequivocally designated by the two-hour excretion of phenolsulphonephthalein alone as a control. It does seem possible to conclude that a diminished excretion of hippuric acid can be anticipated when renal function is depressed.

RESULTS

Forty-nine tests were done on 24 patients. The results are summarized in Table I. Only one case of the 15 patients tested at or near term showed an entirely normal total 4-hour excretion of hippuric acid after sodium benzoate. Five of these patients had in a single hour a normal output of 0.9 gm. or more. Four cases were normal pregnancies by all clinical criteria, the rest of the patients had varying degrees of toxemia as noted in Table I. The average output of hippuric acid was somewhat higher in the normal than in the toxic cases, 79 per cent against 69 per cent respectively. The patients with particularly low output were toxic, yet the one patient at term with a normal output (No. 17) had a mild toxemia. Of those patients on whom a repeat test was obtained on the tenth day postpartum only one had a subnormal return, and it is possible that in this case there was an error in technic, since the analysis was delayed and the urine stood without preservative.

Three patients who were given 7.3 gm. of neutralized hippuric acid by mouth (Nos. 7, 12, and 13) showed a low normal recovery of hippuric acid whereas their output after sodium benzoate was slightly subnormal.

Six of the patients at term were given 2 gm. of hippuric acid as the sodium salt intravenously (Nos. 13, 18, 20, 21, 22, and 23). Four showed rather marked depression of excretion, particularly in the first half hour. One on whom a repeat test was done on the tenth day postpartum (No. 23) showed some improvement but still considerably delayed excretion, although a fifteen-minute fractional phenolsulphonephthalein test done the same day was normal. The two patients who had a normal or but slightly depressed excretion (Nos. 21 and 22) had toxemias developing very late in pregnancy tentatively classified as preeclampsia.

Six tests were done on normal women in the fourth to eighth month of pregnancy. One of these (No. 3) had a slightly low but essentially normal output, another (No. 6) showed a definitely low recovery, the rest were entirely normal. One patient (No. 24) with a tentative diagnosis of chronic nephritis had at the end of the eighth month a low output of intravenous sodium hippurate, but a normal output of hippuric acid after sodium benzoate by mouth.

A patient with severe vomiting and moderate icterus in the third month of gestation (No. 15) showed a definitely impaired synthesis of hippuric acid in a test done after her icteric index was normal, while another test a week later showed improvement.

With the exception of occasional vertigo no untoward reactions occurred from the sodium benzoate. There was no vomiting, though it is unlikely that patients with nausea would be able to tolerate the test until they are able to retain food.

TABLE II. EXCRETION OF HIPPURIC ACID AFTER INTRAVENOUS SODIUM HIPPURATE

CASE	DAY	ONE-HALF HOUR	ONE HOUR	TWO HOURS
13	+ 8	69%	79%	83%
18	- 2	38%	53%	61%
20	- 6	30%	63%	75%
21	+ 1	61%	79%	
22	+ 2	51%	77%	
23	- 1	6%	29%	
	+10	26%	62%	
24	-34	11%	31%	

DISCUSSION

While it is not possible from the information provided to date by this investigation to define the exact status of the synthesis of hippuric acid in pregnancy, nor at present to separate the nephric and hepatic factors, it seems likely that as the majority of women reach term there is a definite disturbance of the excretion of hippuric acid which does not persist through the puerperium. The distinction between the normal and toxic patient's metabolism of benzoic acid is, again, not plain, but in this series the recovery of hippuric acid has been somewhat less in the latter.

A most interesting field of speculation is opened by a consideration of the detoxification and excretion of the aromatic substances, of which benzoic acid is a type.

The nature of the hypothetical toxins that disturb pregnancy is unknown. It is known that toxic aromatic substances occur in the body, for example, as a result of intestinal hydrolysis. If it were possible to demonstrate a failure of the normal mechanisms of detoxification either through a deficiency of the substance, in this instance, glycine, necessary to conjugation (perhaps secondary to hepatic dysfunction) or a depression of renal excretion, another point for attacking the problem would be provided.

One of the more constant chemical findings in the most characteristic of the toxemias of pregnancy, eclampsia, is an elevated blood uric acid. It has long been considered that uricidemia was one of the first evidences of renal deficiency, preceding the retention of other nitrogenous substances. It is now recognized that this is very doubtful.^{11, 12} Quick¹² points out that uric acid excretion tends to be constant but definitely influenced by certain metabolic and toxic materials. Its excretion is increased by substances he designates as anti-ketogenic, e.g., glucose, glycerol, pyruvic acid, glycine, alanine, aspartic and glutamic acids, and by a high protein diet. Excretion is diminished by ketogenic substances: a high fat diet, fasting, acetoacetic acid by mouth, by lactic acid either administered or produced in excess metabolically, and by benzoic, phenylacetic and other aromatic acids. It has been shown already that an increase in lactic acid occurs in eclampsia. It is also suggested that toxins similar to these aromatic acids may be responsible for the decreased elimination of uric acid. Another possibility is the diversion of the amino acids or other anti-ketogenic substance to the fetus.

If the conjugative mechanism should prove to be still adequate, in the presence of a deficiency of the substance with which the toxin is conjugated, for example, glycine, it may be possible to make a therapeutic replacement. Glycine, for one, is readily available as such and is present in high percentage in gelatin. Such substances also may accelerate the excretion of already conjugated aromatic compounds.^{13, 14} It is also worthy of consideration that the low protein dietary treatment of toxemia may, in fact, lead to a deficient intake of these elements, and place a burden on the mechanism of synthesis.

It is felt that a further study of the metabolism of benzoic acid in pregnancy including a more definite determination of the renal threshold of hippuric acid, a parallel study of the blood and urine uric acid levels, and a trial of the effect of high glycine feeding would be profitable.

SUMMARY

1. It is shown that the excretion of hippuric acid after the administration of sodium benzoate is diminished toward the termination of normal and toxemic pregnancies. In some cases there is depressed excretion of sodium hippurate given intravenously.
2. A case of hyperemesis gravidarum showed definite liver dysfunction by this test.
3. The possible relation of the conjugation and excretion of aromatic toxins to uric acid excretion and the toxemias of pregnancy is discussed.

I am indebted to Dr. Armand J. Quick for invaluable technical advice and criticism.

The expenses of this study were borne by the Edwin F. Lindridge Fund.

REFERENCES

- (1) Swanson, W. W.: J. Biol. Chem. 62: 565, 1925. (2) Quick, A. J.: Am. J. Med. Sc. 185: 630, 1933. (3) Stander, H. J.: Medicine 8: 1, 1929. (4) Cross, R. C.: AM. J. OBST. & GYNEC. 18: 800, 1929. (5) Sullivan, C. F., Tew, W. P., and Watson, E. M.: J. Obst. & Gynec. Brit. Emp. 41: 347, 1934. (6) Griffith, W. H.: J. Biol. Chem. 66: 671, 1925. (7) Swick, M.: Surg. Gynec. Obst. 56: 62, 1933. (8) Kingsbury, F. B., and Swanson, W. W.: Arch. Int. Med. 28: 220, 1921. (9) Bryan, A. W.: J. Clin. Investigation 2: 1, 1925. (10) Morgulis, S., Pratt, G. P., and Jahr, H. M.: Arch. Int. Med. 31: 116, 1923. (11) Johnston, C.: J. Clin. Investigation 9: 555, 1931. (12) Quick, A. J.: M. Clin. North America 17: 1325, 1934. (13) Quick, A. J.: J. Biol. Chem. 92: 65, 1931. (14) Quick, A. J.: J. Biol. Chem. 98: 157, 1932.

A STUDY OF BLOOD SUGAR LEVELS IN ECLAMPSIA

C. R. MAYS, M.D., AND W. M. MCCORD, PH.D., NEW ORLEANS, LA.

(From the Departments of Gynecology and Biochemistry Louisiana State University Medical Center and the State Charity Hospital.)

IN RECENT articles on the treatment of eclampsia there appears an increasing use of dextrose in the treatment of pregnancy toxicosis. There still exists, however, some controversy on the rationale of this therapeutic procedure. Various methods of administration and doses

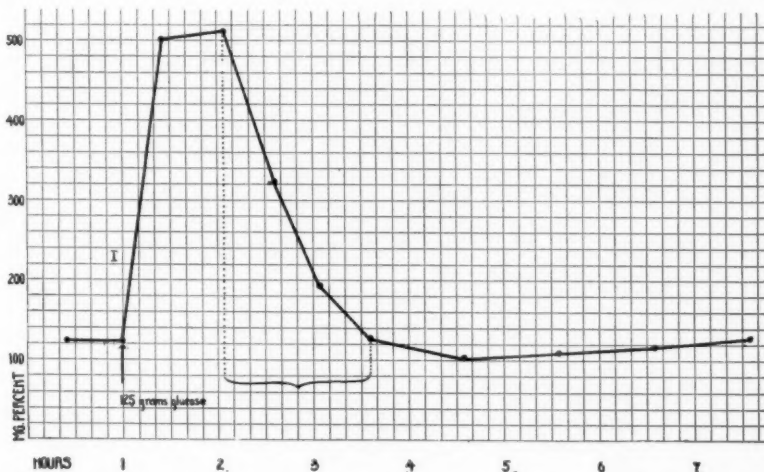


Fig. 1.—Case 1. Samples taken at thirty-minute intervals.

Period	Time	Avg. Fall	Convulsions	Sugar Conc.
1	1 hr. 30 min.	258.0 mg. per hr.	—	—

have been recommended based upon a variety of theories regarding the beneficial effects of dextrose infusions. For this reason we have studied the influence of blood sugar concentration on the incidence of convulsive manifestation of eclampsia.

We have favored the use of dextrose in the treatment of our eclamptic patients for its protective influence against liver degeneration and the strong diuretic effect it produces. The diuretic efficiency of dex-

trose must be directly proportional to the molecular concentration that it reaches in the circulating blood and the duration of time that is held at this given high level.

In the selection of cases for this study only those patients which showed convulsive manifestations of eclampsia, immediately preceding the period of observation were employed. Medication, other than

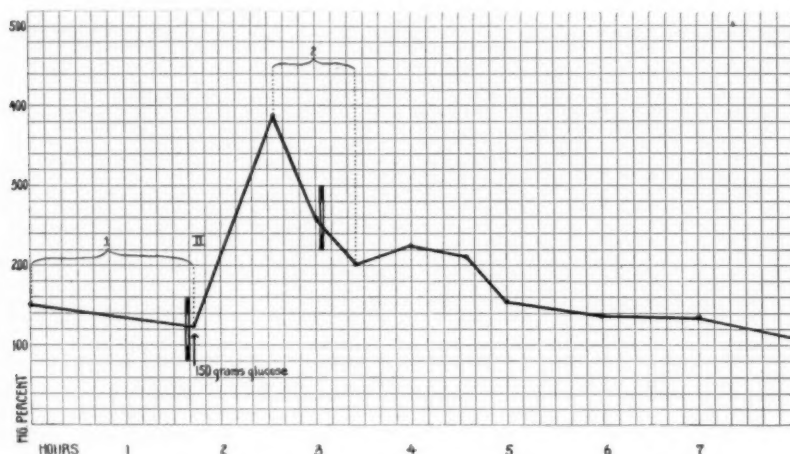


Fig. 2.—Case 2. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	1 hr. 43 min.	21.5 mg. per hr.	1	at 122 mg. %
2	50 min.	222.0 mg. per hr.	1	at 250 mg. %

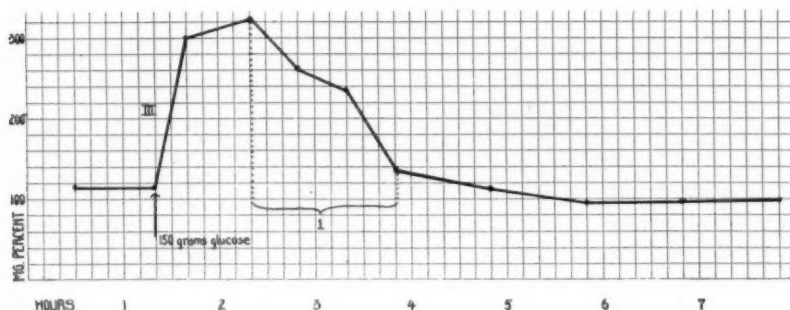


Fig. 3.—Case 3. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	1 hr. 30 min.	124.0 mg. per hr.	—	—

insulin and glucose, was not administered during the experimental period except in three cases, a notation of which is made in the case report.

During the earlier studies (Cases 1, 2, 3, 4, and 6) the blood sugar determinations were made upon capillary blood from the finger tips by the method of Folin and Malmros.¹ In the remainder of the series blood was obtained from the median vein and preserved in tubes containing oxalate and floride² in the ice box until analyzed eight or ten hours afterward at the latest. The blood proteins were precipitated according to Somogyi³ and the sugar determined by the method of Folin.⁴

RESULTS

In Table I is presented the blood sugar concentrations at the beginning of the study. Our data are presented in Figs. 1 to 14. Analysis of these charts may be found in Table II.

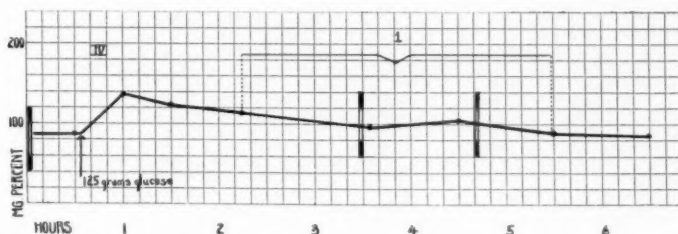


Fig. 4.—Case 4. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	3 hr. 15 min.	8.5 mg. per hr.	2	at 100 mg. %

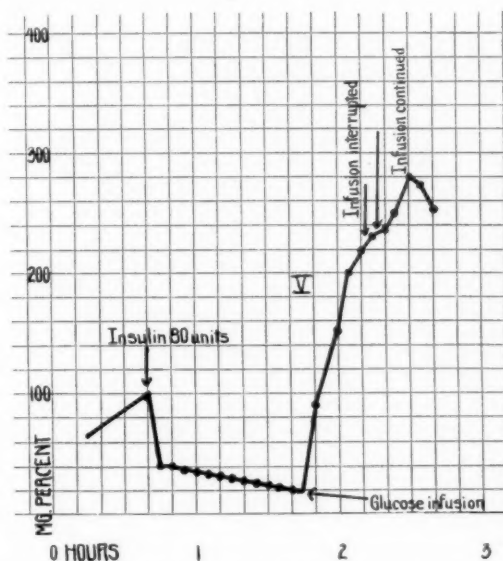


Fig. 5.—Case 5. Samples taken at five-minute intervals. After initial drop curve is smooth with no abrupt changes until glucose infusion was interrupted for a few moments and until peak was reached.

DISCUSSION

In the analysis of our material we find that due to the rapid administration of dextrose most of our time was spent in the study of blood sugar values during their declining periods. It is, therefore, probable that irrespective of the effect of increasing and decreasing blood sugar levels on the incidence of convulsions, the mathematical possibility of convulsions occurring during the declining periods of our graphs is greatly increased over the possibility of their occurrence during increasing glyceemic levels.

TABLE I. GLYCEMIC LEVEL ON ADMISSION

HYP0	NORMAL	HYPER	
89	105	125	
	116	121	
1	2	2	Av. 111.2
Folin-Wu Normal—90-120			
69	96		
64	93	395	
	72	273	
	78	148	
2	4	3	Av. 142.9
Somogyi-Folin Normal—70-100			

TABLE II. AVERAGE RATE OF FALL IN BLOOD SUGAR CONCENTRATION AND INCIDENCE OF CONVULSIONS.

	AVERAGE RATES OF FALL	NO. OF CONVULSIONS	SUGAR CONC. MG. %
Group I. Receiving no insulin.			
Case 1	258.0	—	—
Case 2	21.5	1	112
	222.0	1	250
Case 3	124.0	—	—
Case 4	8.5	2	100
Group II. Receiving insulin			
Case 5	—	—	—
Case 6	225.0	1	170
	50.0	1	110
Case 7	40.0	1	250
	188.0	—	—
	40.0	1	120
Case 8	0.0	1	93
	39.0	1	34
Rise	1098.0	—	—
	140.0	—	—
Case 9	0.0	1	148
	20.0	1	57
Case 10	204.0	—	—
Case 11	26.0	—	—
	6.0	—	—
Rise	384.0	—	—
	313.0	1	470
	64.0	1	330
	64.0	1	265
Case 12	200.0	—	—
	9.0	2	202
Rise	810.0	—	—
	188.0	1	700
	188.0	1	690
Case 13			
Rise	29.0	1	93
	52.0	1	93
Rise	137.0	1	382
Rise	112.0	1	340
Case 14	0.0	1	96
	24.0	1	90
	15.5	1	65
Rise	314.0	1	580
Rise	64.0	1	678
	46.0	1	636

In that the occurrence of convulsions has been suggested to be due to a relative hypoglycemia, that is, a rapid fall in blood sugar level from a preexisting higher level to a lower level, regardless of the

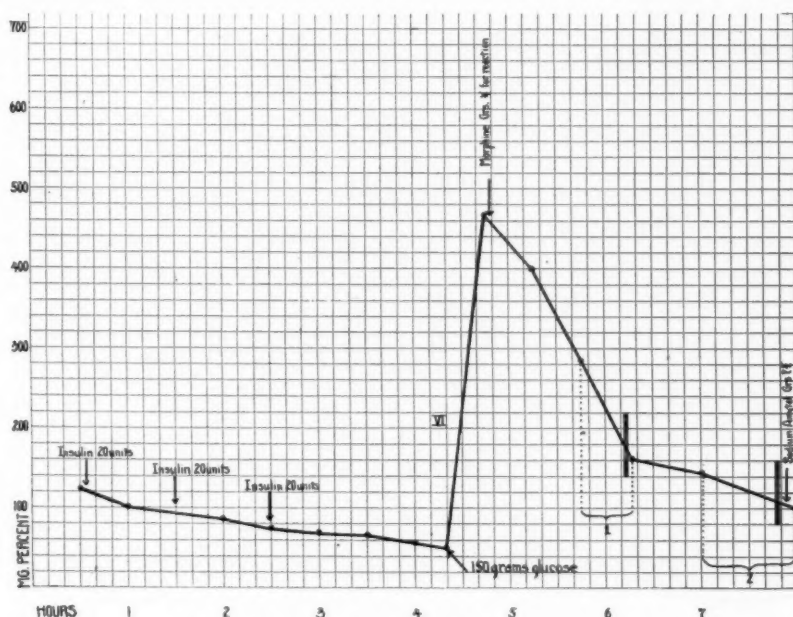


Fig. 6.—Case 6. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	33 min.	225.0 mg. per hr.	1	at 170 mg. %
2	1 hr.	50.0 mg. per hr.	1	at 110 mg. %

(Medication—Morphine and sodium amytal)

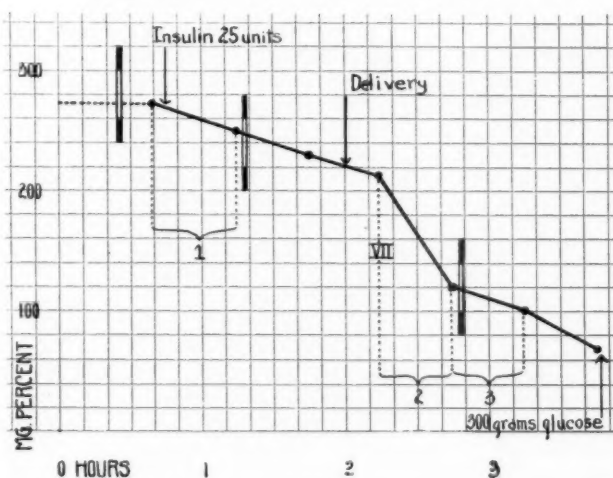


Fig. 7.—Case 7. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	35 min.	40.0 mg. per hr.	1	at 250 mg. %
2	30 min.	188.0 mg. per hr.	1	at 120 mg. %
3	30 min.	40.0 mg. per hr.	1	at 120 mg. %

absolute level, we have first selected a series of four cases which exhibited convulsive manifestations of eclampsia immediately preceding the study in which we gave rapid infusion of large doses of dextrose.

In Cases 1 and 3 it may be seen that no convulsions occurred during the decline in blood sugar concentration. Case 1 is especially convincing because of the rapid

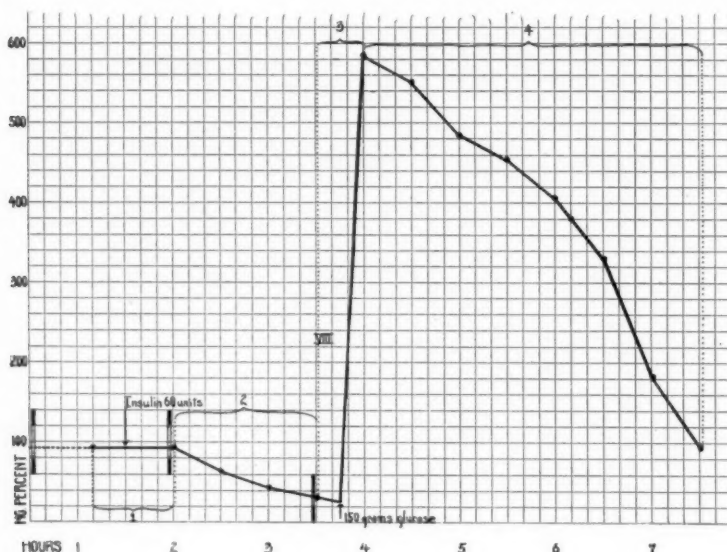


Fig. 8.—Case 8. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	50 min.	0.0 mg. per hr.	1	at 93 mg. %
2	1 hr. 30 min.	39.0 mg. per hr.	1	at 34 mg. %
	30 min.	Rise of 1098 per hr.	—	—
	3 hr. 30 min.	140.0 mg. per hr.	—	—

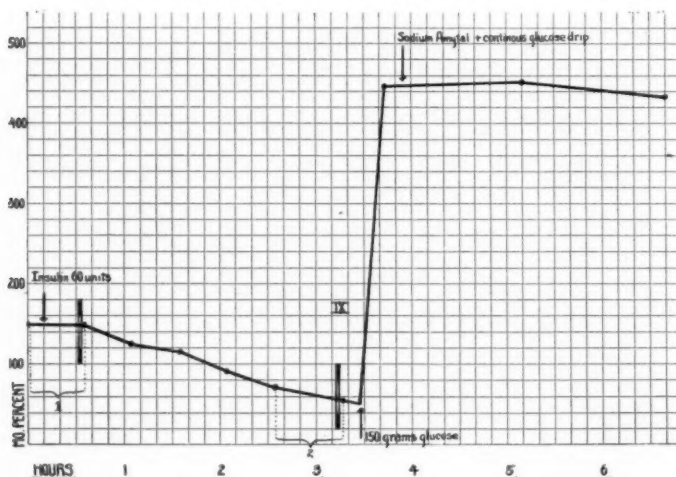


Fig. 9.—Case 9. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	35 min.	0 mg. per hr.	1	at 148 mg. %
2	43 min.	20 mg. per hr. (Sodium amytal)	1	at 57 mg. %

decline in blood sugar value to a relatively subnormal value. In Case 2 the incidence of convulsions was not increased in proportion to the rapidity of decline in blood sugar levels. In Case 3 although there was a slower rate of decline in blood sugar, the incidence of convulsions was greater than in Case 2.

A study of the remaining charts shows, as summarized in Table II, that there is no relationship between the incidence of convulsions and the rapidity in which rela-

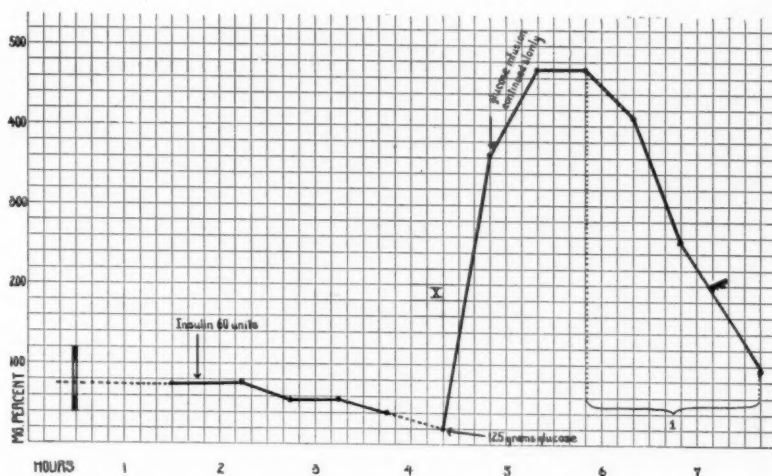


Fig. 10.—Case 10. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	1 hr. 50 min.	204 mg. per hr.	—	—

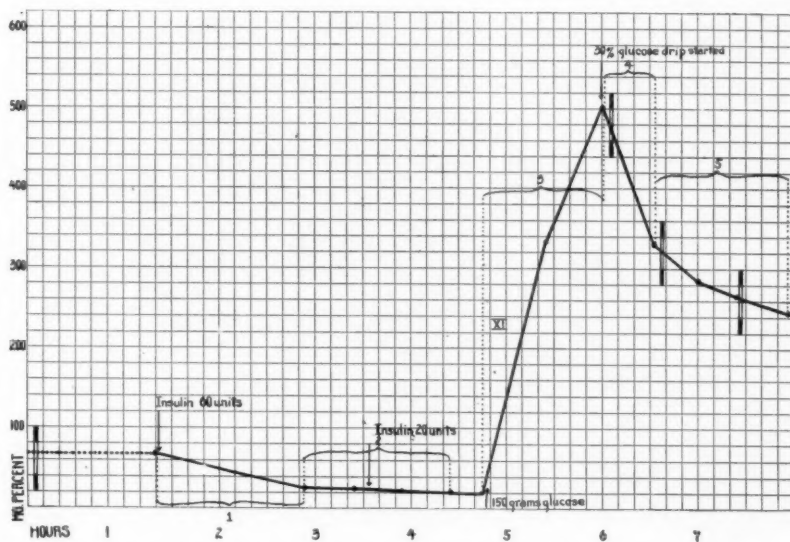


Fig. 11.—Case 11. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	1 hr. 35 min.	26 mg. per hr.	—	—
2	1 hr. 30 min.	6 mg. per hr.	—	—
3	1 hr. 15 min.	Rise of 384 mg. per hr.	—	—
4	32 min.	313 mg. per hr.	1	at 470 mg. %
5	1 hr. 25 min.	64 mg. per hr.	1	at 330 mg. %
			1	at 265 mg. %

tive hypoglycemic levels are sought as has been contended. Cases 6, 11, 13, and 14 showed no increased tendency, to develop convulsions, as the blood sugar was forced from its original level to absolute hypoglycemic levels as compared to the periods during which the blood sugar sought to return to its original level from an absolute hyperglycemia after glucose infusion. Case 8 on the other hand shows a convulsion during a declining period to an absolute hypoglycemia and yet shows no convulsions during a declining period from an absolute hyperglycemia of 580 mg. per cent. When compared with Case 11 we cannot see that this phenomena is of any significance in that the two charts show exactly opposite effects. In the analysis of cases in which the blood sugar was lowered by the use of insulin we find that fifteen convulsions occurred at normal or lower than normal values and seventeen occurred at definitely high values. Convulsions occurred irrespective of the blood sugar concentration ranging from 34 mg. per cent in Case 8 to 705 mg. per cent in Case 12.

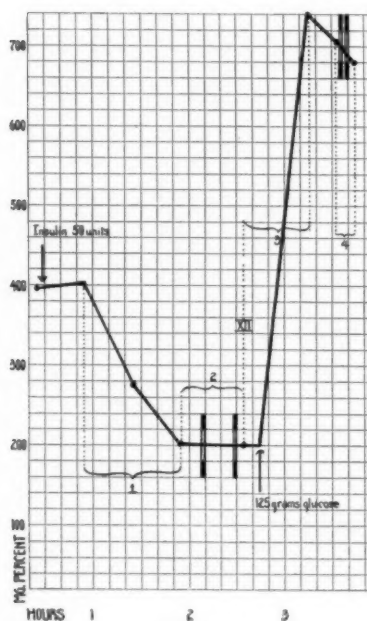


Fig. 12.

Fig. 12.—Case 12. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	1 hr.	200 mg. per hr.	—	—
2	40 min.	9 mg. per hr.	2	at 202 mg. %
3	40 min.	Rise of 810 mg. per hr.	1	at 700 mg. %
4	8 min.	188 mg. per hr.	1	at 690

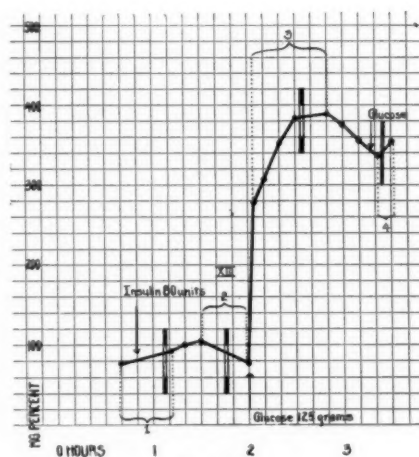


Fig. 13.

Fig. 13.—Case 13. Samples taken at ten-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	31 min.	Rise of 29 mg. per hr.	1	at 93 mg. %
2	30 min.	52 mg. per hr.	1	at 93 mg. %
3	48 min.	Rise of 137 mg. per hr.	1	at 382 mg. %
4	8 min.	Rise of 112 mg. per hr.	1	at 340 mg. %

In view of the fact, as we have previously mentioned, that it is improbable that a convulsion should occur during the rise in blood sugar concentration during the early periods of glucose infusion, we finally present Cases 13 and 14, in which convulsions occur during periods of rapid increase in blood sugar concentration.

The irregular fluctuations in blood sugar in eclampsia, we think, have been indisputably presented. We are inclined, however, to agree with Stander and Harris⁵ that many of these minor fluctuations might perhaps be attributed to error inherent in blood sugar determinations. This has been demonstrated by Seigle and Wiley⁶ who show errors ranging from 1.1 per cent to over 20 per cent with variations of 0.5 mm. on the scale reading. We also observed during the collection of specimens that the patients were extremely restless and not infrequently had to be restrained. We believe this might at least produce a noticeable variation from time to time. We, therefore, have made an observation of the variations in the blood sugar concentration of



Fig. 14.—Case 14. Samples taken at thirty-minute intervals.

Period	Time	Av. Fall	Convulsions	Sugar Conc.
1	38 min.	0.0 mg. per hr.	1	at 96 mg. %
2	30 min.	24.0 mg. per hr.	1	at 90 mg. %
3	1 hr. 17 min.	15.5 mg. per hr.	1	at 65 mg. %
4	30 min.	Rise of 314 mg. per hr.	1	at 580 mg. %
5	30 min.	Rise of 64 mg. per hr.	1	678 mg. %
6	55 min.	46.0 mg. per hr.	1	(min. later) at 636 mg. %

(Sodium amytal)

a normal primipara which data may be found in Table III. This patient in no way approached the emotional excitability and muscular activity of our eclamptic cases, and yet still showed a variation of 15 mg. per cent over the course of an hour. Although we do not feel that conclusions are justified from this single observation, we suggest that the fluctuations which have been observed in eclampsia may be due to muscular activity and might be observed in a normal patient under the same conditions of excitement and activity.

TABLE III. BLOOD SAMPLES TAKEN AT FIVE-MINUTE INTERVALS. GLUCOSE DETERMINED BY METHOD OF FOLIN ON SOMOGYI FILTRATE.

NORMAL PRIMIPARAS AT MIDDLE OF FIRST STAGE OF LABOR

TIME	BLOOD SUGAR CONCENTRATION
0 min.	84
5	76
10	79
15	74
20	75
25	74
30	74
35	78
40	69
45	75
50	74
55	78

CONCLUSIONS

1. Neither hypo- nor hyperglycemia is characteristic of eclampsia. The blood sugar concentration probably depends upon the patient's nutritional state and the degree of emotional stability and muscular activity immediately preceding the taking of the specimen.

2. The absolute blood sugar concentration has no effect whatsoever on the incidence of convulsions.

3. Convulsions occur independently of the rate of decline in blood sugar concentrations.

4. Convulsions occur during a rapid rise in blood sugar concentration as well as during a rapid decline.

REFERENCES

- (1) *Folin, O., and Malmros, H.*: J. Biol. Chem. **77**: 421, 1928; **83**: 115, 1929.
 (2) *van der Walle, N., and Noeridin, R.*: Geneeskund Tijdschr. Nederland. Indie. **73**: 480, 1933. (3) *Somogyi*: J. Biol. Chem. **70**: 599, 1926; **86**: 655, 1930. (4) *Folin, O.*: J. Biol. Chem. **82**: 83, 1929. (5) *Stander, H. J., and Harrison, E. P. H.*: AM. J. OBST. & GYNEC. **18**: 17, 1929. (6) *Siegel, I. A., and Wylic, H. B.*: AM. J. OBST. & GYNEC. **26**: 29, 1933.

Vignes, H.: The Treatment of Hydramnios, Bull. Soc. d'obst. et de gynéc. page 45, 1933.

Vignes treated a primipara who had hydramnion with calomel suppositories and intramuscular injections of iodized oil for almost twelve weeks until labor set in. By means of a graph he demonstrates the effect this medication had in stabilizing the height of the uterus. Labor was normal and a normal child weighing 3,800 gm. was delivered. The father of the child was found to have leucoplakia and unequal pupils. The placenta on histologic examination demonstrated changes almost certainly indicative of syphilis.

J. P. GREENHILL.

CONGENITAL ANEMIA OF THE NEWBORN

HARRY D. PASACHOFF, M.D., AND LEO WILSON, M.D., NEW YORK, N. Y.

*(From the Departments of Obstetrics and Pediatrics of the
Morrisania City Hospital)*

DURING the past few years a newly described form of anemia affecting newborn infants has attracted attention in the pediatric literature. Since the obstetrician has the first opportunity to observe the disorders of the neonatal period, we hope that his interest in this obscure disease will be stimulated. Early recognition and prompt institution of the proper treatment may be life saving.

Congenital anemia of the newborn may be defined as a hyperchromic anemia of unknown etiology that appears at birth or within the first two weeks of life in full-term and premature infants born of healthy parents. Since 1919, when Ecklin first described a case of unexplained anemia in a newborn infant, approximately fifty cases have been reported in the literature from this country and abroad.

INCIDENCE

At the Morrisania City Hospital we found three cases in 6,000 births. The clinical diagnosis was made on the appearance of marked pallor. Perhaps, in addition, several mild cases might have been discovered if blood counts had been performed routinely on all newborn infants.

The anemia usually makes its appearance between the third and the tenth day of life. In some cases the anemia has been noted at birth. Both sexes are equally affected. All recorded cases have been in the white race. We report here for the first time a case in a negro infant. The occurrence of congenital anemia of the newborn in several offsprings of the same parents has been noted a number of times including one report in three successive siblings. It has been described in one of twins. With the exception of two cases reported by Akerren, no cases have been recorded in which congenital anemia occurred in the first born. Why the first born is spared is at present unexplained.

The familial association of congenital anemia and of icterus gravis neonatorum has been noted several times. We recently reported a case in which congenital anemia and universal hydrops of the fetus occurred in successive siblings.

SYMPTOMATOLOGY

Pallor is the only characteristic symptom of congenital anemia of the newborn. This may appear at any time within the first two weeks

of life, and early, may be masked by jaundice. However, when the jaundice clears, the waxy yellow color becomes evident. Icterus is not a constant symptom. It has been noted in about one-half of the reported cases. It appears earlier than the physiologic icterus of the newborn and is usually mild. Vomiting is a frequent symptom. In isolated instances edema of the eyes and of the scrotum has been noted. Petechiae and purpuric spots have occurred in a few cases. Occasionally the liver and spleen have been markedly enlarged. The spleen has been palpable in only about one-half of the reported cases. Hypertrophy of the heart has been noted in a few instances.

Despite the intense anemia the infant does not appear to be very sick. He takes his feedings well and usually gains in weight. There is no fever and no gross bleeding. With recovery all symptoms promptly disappear. The liver, spleen and heart rapidly return to normal size. The pallor persists somewhat longer. Recovery is complete by the third to the sixth month. Some cases which have been followed for several years have shown no late sequelae.

DIAGNOSIS

All causes of secondary anemia must be excluded. Among the more frequent of these are congenital syphilis, sepsis, and hemorrhagic disorders. Much more rarely icterus gravis neonatorum, neoplasms, congenital malformations of the cardiovascular system, tuberculosis, diphtheria, and malaria are responsible for anemia in the neonatal period.

BLOOD PICTURE

In the normal newborn infant the erythrocyte count ranges from 5,000,000 to 8,000,000; the hemoglobin is correspondingly high (95 per cent to 120 per cent). The blood picture in congenital anemia is of the hyperchromic type. The degree of anemia varies considerably. The most severe case recorded was reported by us (hemoglobin 8 per cent; erythrocytes 400,000). The erythrocytes are large and well filled with hemoglobin, giving a color index of 1 or above. Anisocytosis and poikilocytosis are usually marked. Polychromatophilia, basophilic stippling, normoblasts, megaloblasts, Cabot ring bodies, and reticulocytes may be present early but usually become more marked with the beginning of recovery. When improvement is well established these signs of blood regeneration rapidly disappear.

The leucocyte count is generally within the normal range of 10,000 to 25,000 although a slight degree of leucocytosis may occur. The differential count, platelets, bleeding and coagulation time and the fragility tests are normal. Early in the disease the icteric index is increased.

PATHOLOGY

Four detailed autopsy protocols including one of our own have been reported. Two cases showed marked erythropoietic activity in the bone marrow and extramedullary foci (Susstrunk, Schleussing). One case showed few erythrocytes or erythroblasts in the bone marrow but considerable erythroblastic activity in the liver and spleen (Happ). In our fatal case there was no evidence of erythroblastosis. The liver and spleen showed a myeloid hyperplasia. Petechial hemorrhages were present in three of the four cases.

ETIOLOGY

In general, the theories fall into one of two groups: (a) Defective blood formation; (b) Excessive blood destruction.

Defective Blood Formation.—1. *Nutritional deficiency:* This theory is based on the assumption that the mother's diet during pregnancy has been inadequate in blood-forming elements. There is no evidence to support this theory. 2. *Toxin production:* A theoretical possibility but also with no evidence in its support is that a toxin arising from either the mother or the fetus depresses the activity of the blood-forming organs. The general good health of the mother and child speak against this theory. 3. *Congenital hematopoietic hypofunction:* The development of the erythropoietic system during fetal life does not keep pace with the other systems of the body so that at birth when the latter are fully developed, the erythropoietic system is still in the fetal stage. A modification of this theory is that at birth or shortly after there is a temporary inhibition of the usual activity of the hematopoietic system. Anemia develops because the normal destruction of mature red cells continues but no new cells are produced to compensate for the loss. 4. *Erythroblastosis:* According to this concept there is a persistence or a reversion to the embryonic level of blood formation due to a primary metabolic disturbance of the hematopoietic system. The result is that immature nucleated red cells are released into the peripheral circulation in large numbers and undergo early destruction.

Excessive Blood Destruction.—*Hemolysis* has been suggested as a possible cause of anemia in the newborn. The frequent absence of jaundice is explained by the ability of the liver to excrete the pigment.

PROGNOSIS AND TREATMENT

There is a striking tendency to spontaneous recovery. The mortality rate in the reported cases is approximately 12 per cent. Many mild cases are probably unrecognized and recover without treatment.

Moderately severe cases, with hemoglobin above 30 per cent, also often show a steady improvement without therapy. If the hemoglobin falls below 30 per cent, immediate transfusion is imperative. Transfusion must be repeated if continued improvement does not follow. A number of cases have required two or three transfusions.

Iron, liver extract and quartz lamp therapy have been used with apparent success, but it is difficult to gauge their therapeutic value because the disease has a decided tendency to spontaneous improvement. There does not seem to be an iron deficiency (Case 3). In this case the infant made a complete recovery without therapy and on breast milk feeding which is poor in iron.

CASE REPORTS

CASE 1.—E. P., a white full-term infant, the second child of healthy parents, was born on May 26, 1930, after an easy breech delivery. The birth weight was 7 pounds 5 ounces. Jaundice and pallor were noted on the second day. As the jaundice gradually diminished, the skin assumed a waxy yellow appearance. The spleen was palpable. Blood examination on the fifth day showed: erythrocytes 400,000, hemoglobin 8 per cent, color index 1.0, platelets 242,000, coagulation time five and one-half minutes, bleeding time twenty-two minutes, leucocytes 16,880 with polynuclears 25 per cent, lymphocytes 53 per cent, metamyelocytes 13 per cent, myelocytes 7 per cent, and monocytes 2 per cent. There was an occasional normoblast but no megaloblasts. A transfusion was ordered but the baby had a sudden collapse and died within an hour. At postmortem examination there was found a myeloid hyperplasia of the liver, spleen, and bone marrow with almost complete absence of erythropoiesis.

Two subsequent pregnancies in the same mother resulted in premature stillbirths showing universal edema. Autopsy performed on the second fetus showed, on gross inspection, generalized edema with fluid in the various body cavities. Microscopic sections failed to show evidence of increased erythroblastic activity.

Comment.—We have reported these cases in detail elsewhere including illustrations of the histologic sections. We repeat this brief summary here to point out several important features. The association of these two diseases in siblings points to a common etiologic factor and a familial association. There was an absence of abnormal erythroblastic activity in both the cases of congenital anemia of the newborn and of universal edema of the fetus. This case of congenital anemia represents the severest form. Possibly earlier recognition and treatment would have resulted in recovery of the patient.

CASE 2.—P. H., a white full-term male infant, was the fourth child of healthy parents. The first two children are well. The third pregnancy terminated in the birth of a macerated fetus one month prior to term. The prenatal course in the fourth pregnancy was normal. The delivery was spontaneous. The infant weighed 7½ pounds at birth and appeared normal. Jaundice was noticed on the second day; and pallor was noted on the sixth day. The liver was palpable 3 cm. below the costal margin and the spleen was down to the umbilicus. There was no vomiting, edema, bleeding, or fever. The mother's blood count was normal and the Wassermann test was negative.

Blood count on the eighth day showed: erythrocytes 1,200,000, hemoglobin 29 per cent, color index 1.2, and leucocytes 25,000. Differential count showed polynuclears

50 per cent, lymphocytes 43 per cent, monocytes 2 per cent, myelocytes 4 per cent, myeloblasts 1 per cent. There were 16 normoblasts per 100 white cells counted. The smear showed moderate anisocytosis, poikilocytosis and polychromatophilia.

Transfusion of 30 c.c. of blood was given with considerable but only temporary improvement. Another transfusion of 40 c.c. was given one week later. Improvement was now sustained and no further treatment was required. Following the second transfusion, the child developed an upper respiratory infection complicated by a bilateral otitis media which cleared up promptly. At the age of five months there was a recurrence of the middle ear infection. At six months, the red blood cell count was 5,570,000 and the hemoglobin 105 per cent. The weight curve has

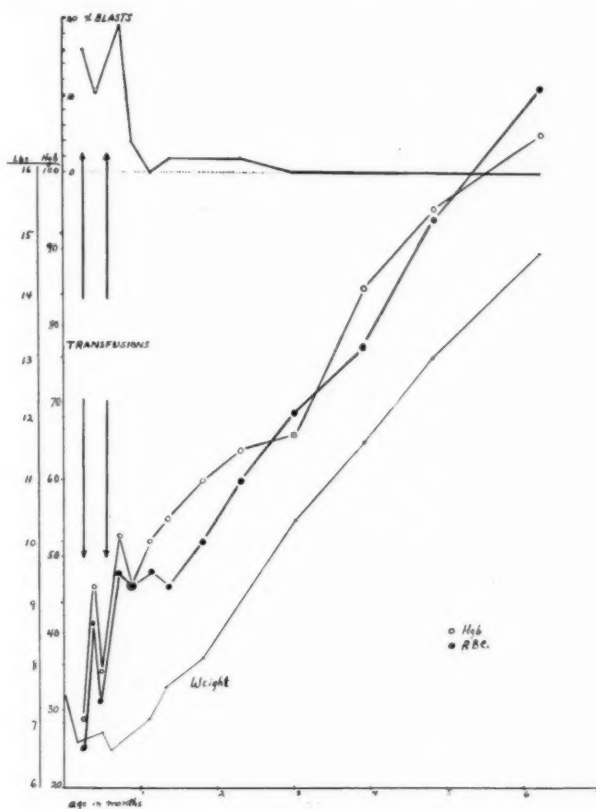


Fig. 1.—Case 2.

also paralleled the erythrocyte and hemoglobin curves. The normoblasts rapidly disappeared from the peripheral blood.

Comment.—This case is a typical severe form of congenital anemia of the newborn. The presence of 16 normoblasts per hundred white cells indicates an active attempt at regeneration. It required two transfusions to give the proper impetus to normal erythropoiesis.

CASE 3.—O. B., a full-term male infant, was the third child of healthy negro parents. The first two children are alive and well. The third pregnancy was uneventful and terminated on Oct. 1, 1933, in the spontaneous delivery of an infant weighing 6½ pounds who appeared normal at birth. The mother's blood count was normal and the blood Wassermann test on both parents was negative. On the

eighth day it was noted that the infant was pale. The liver and spleen were not palpable but the heart was slightly enlarged.

Blood count on the ninth day showed: erythrocytes 1,480,000, hemoglobin 38 per cent, color index 1.3, leucocytes 14,150. Differential count showed: polynuclears 52 per cent, lymphocytes 46 per cent, monocytes 1 per cent, and myelocytes 1 per cent. There was one normoblast per one hundred white cells counted. The smear showed slight anisocytosis, poikilocytosis and polychromatophilia. Repeated examination of wet blood smears failed to show any sickling of the red cells.

The infant was breast fed and kept under observation at home without any treatment. At twenty days, the red blood cell count had risen to 2,270,000 and the

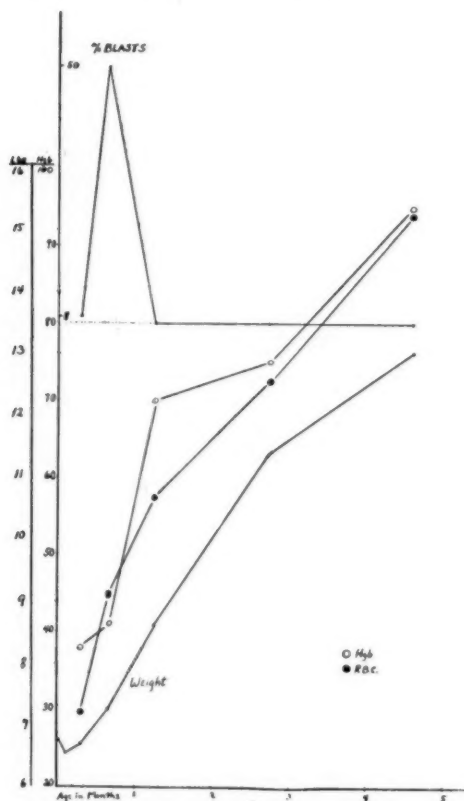


Fig. 2.—Case 3.

hemoglobin was 41 per cent. The striking feature, however, was the very marked evidence of regenerative activity present in the blood smear at this time. There were 50 nucleated red cells per one hundred white cells of which 90 per cent were normoblasts and the remainder megaloblasts. In addition, marked polychromatophilia, basophilic stippling and numerous Cabot ring bodies were present.

Seventeen days later, the hemoglobin had risen to 70 per cent and the erythrocytes to 2,870,000. No nucleated red blood cells were seen. The weight curve also continued to rise. At four and one-half months, the blood count showed a hemoglobin of 95 per cent and erythrocyte count of 4,750,000.

Comment.—This is the first recorded instance in which congenital anemia of the newborn occurred in a negro infant. No evidence of sickle-cell anemia was present. The occurrence of 50 nucleated red cells per 100 white cells at twenty days of age

as compared with one at eight days of age would seem to indicate that erythroblastemia is a secondary response rather than the basic pathologic disorder. Furthermore this case illustrates that recovery may occur without any therapy and despite an iron poor diet.

CASE 4.—L. K., a normally appearing full-term infant, was delivered by median forceps on Feb. 21, 1934. She was the second child, the first being a stillborn following a placenta previa. Her birth weight was 8 pounds 13 ounces. Soon after birth it was noticed that she was pale but no particular significance was attached to this observation. She took her feedings well but did not gain. We saw this baby for the first time at the age of twenty days. Her weight was 8 pounds 5 ounces.

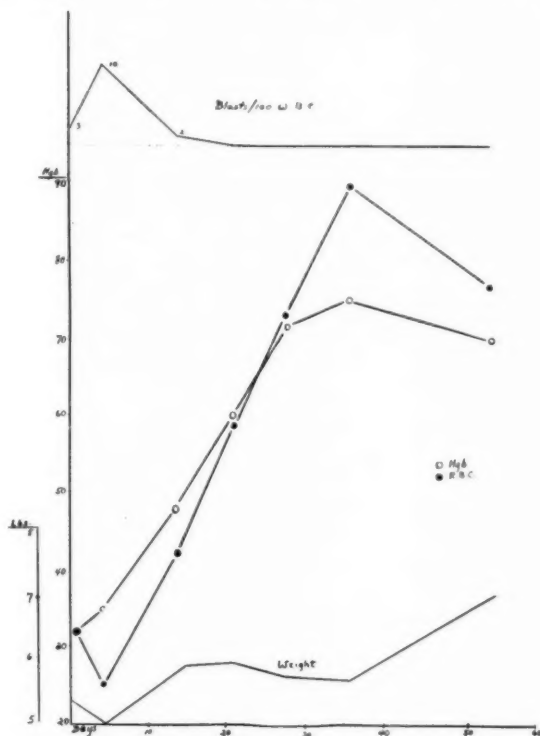


Fig. 3.—Case 5.

She appeared definitely pale. There was no history of jaundice. The physical examination revealed no abnormalities except a healing fracture of the clavicle. The liver and spleen were not enlarged. Blood examination on the same day showed: erythrocytes 2,950,000, hemoglobin 72 per cent (Sahli), color index 1.2, reticulocytes 6 per cent, no nucleated red blood cells, moderate anisocytosis and poikilocytosis, slight polychromatophilia, leucocytes 11,350, lymphocytes 57 per cent, polynuclears 39 per cent, eosinophiles 2 per cent, and monocytes 2 per cent. Platelets were abundant on smear. The bleeding time was three minutes and the coagulation time four minutes.

Comment.—This case, which has just come under our observation, is cited to illustrate the mild type of congenital anemia of the newborn, usually overlooked, and one that recovers spontaneously. Its practical importance is that the infants of future pregnancies in this mother require close watching. Early discovery of a

severe anemia or icterus gravis neonatorum in a subsequent pregnancy with prompt transfusion may become a life-saving measure.

CASE 5.—F. McC., a white male infant weighing 3 pounds 15 ounces, was born on Aug. 24, 1930, three weeks prior to term. The mother had one previous pregnancy in 1929 which resulted in a miscarriage. Both parents were in good health. About a month before the expected termination of the present pregnancy, the mother developed a mild toxemia and labor was induced a few days later. Delivery was spontaneous and the puerperium uneventful. The Wassermann test of the blood of the mother and the infant was negative.

The infant appeared to be fairly sturdy at birth; it took its feedings well and gained in weight. There was no jaundice. During the second week, however, pallor

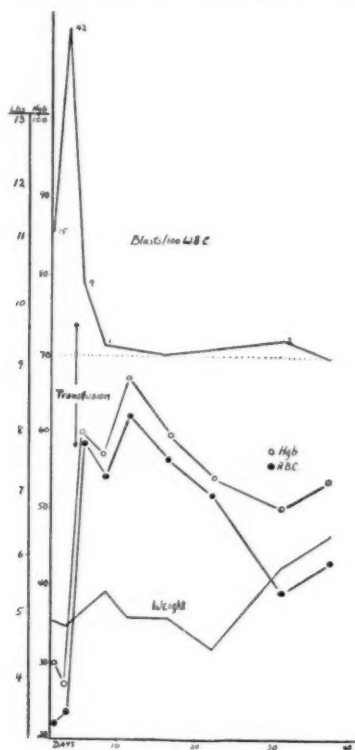


Fig. 4.—Case 6.

gradually developed. The infant was sent home when it was three weeks old and weighed five pounds. One week later, it was readmitted to the hospital because of vomiting and dehydration (pylorospasm). Pallor was now very pronounced. The spleen was palpable 3 cm. below the costal margin but the liver was not enlarged. The vomiting was soon controlled with atropine although a mild fever was present during the administration.

The first blood count, performed when the infant was one month old, showed: erythrocytes 1,600,000, hemoglobin 32 per cent (Sahli), color index 1.0, leucocytes 15,000, lymphocytes 62 per cent, polynuclears 30 per cent, monocytes 4 per cent, and myelocytes 4 per cent. The platelet count was 250,000; the bleeding time, four minutes; and the coagulation time, four minutes. The smear showed 2 normoblasts per 100 white cells counted and moderate polychromatophilia, anisocytosis, and poikilocytosis.

The infant was given short daily exposures of ultraviolet ray and 15 c.c. of whole blood intramuscularly for ten days. Preceding the rapid rise in the erythrocyte count and hemoglobin, there was a transient increase of the normoblasts to 10 per hundred white cells. The spleen soon decreased in size. When the infant was three months old, the erythrocyte count had risen to 3,850,000 and the hemoglobin to 70 per cent.

Comment.—A blood count was not made until the infant was one month old although pallor was noted during the second week of life. The toxemia of pregnancy in this mother was probably coincidental. Although congenital anemia usually occurs in full-term infants, several instances in premature infants have been reported. Congenital anemia in premature infants should not be confused with the anemia of prematurity which does not appear until after the third month.

CASE 6.—E. K., a white female infant weighing 4 pounds 7 ounces, was born on March 8, 1934, six weeks prior to term. Both parents were in good health. The mother had one previous pregnancy in 1932, which resulted in a miscarriage at the fourth month. When the infant was three days old, it became moderately jaundiced. On the seventh day, it appeared to be very pale. The baby was admitted to the hospital one week later. At this time, the skin was a waxy-yellow color and the liver and spleen were palpable just below the costal margin. The weight was 5 pounds. Blood count on April 4, 1934 showed: erythrocytes 1,100,000, hemoglobin 30 per cent (Sahli), color index 1.3; leucocytes 31,600, polynuclears 27 per cent, lymphocytes 68 per cent, myelocytes 4 per cent, and monocytes 1 per cent. There were 15 normoblasts per hundred white cells counted. The smear showed marked polychromatophilia, poikilocytosis, and anisocytosis, and a few Cabot ring bodies. Blood Wassermann test of both parents and the infant was negative. Blood count of the mother was normal. Two days later, the nucleated erythrocytes had increased to 44 per hundred white cells. The infant was given a transfusion of 55 c.c. of citrated blood through the anterior fontanel on the following day. This was followed by a rise of the erythrocytes to 2,950,000 and of the hemoglobin to 60 per cent. A few days later the jaundice disappeared, the liver and spleen were no longer palpable, and the general appearance of the infant was greatly improved.

Comment.—This is another instance of congenital anemia of the newborn in a premature infant. Here again the increase in erythroblasts in the blood two days following the first blood count is striking, and probably signifies an attempt at spontaneous recovery. Because of the severity of the anemia, however, it was deemed safer to transfuse this infant without delay.

SUMMARY AND CONCLUSIONS

An increasing number of instances of congenital anemia of the newborn appearing in the pediatric literature seems to indicate that the disease is more common than was at first believed. We desire to bring this disease to the attention of the obstetrician. Early recognition and prompt institution of appropriate therapy will result in the saving of lives.

Congenital anemia of the newborn is described from the clinical, pathologic, and hematologic viewpoints. The familial tendency is noted, as is also the association with icterus gravis neonatorum and with universal edema of the fetus.

The etiology is unknown. It seems to us that the most attractive theory is that of inhibition of the development of the erythropoietic

system. Erythroblastemia appears to be a secondary response to the anemia rather than the underlying pathology.

Five previously unreported cases are described including the first recorded instance in a negro infant.

REFERENCES

- (1) A review and tabulation of the cases reported up to 1931 will be found in: *Pasachoff, H. D., and Wilson, L.*: *Am. J. Dis. Child.* 42: 111, 1931. *Abt, A. F.*: *Am. J. Dis. Child.* 43: 337, 1932. (2) An analytical review of erythroblastosis fetalis and related diseases including congenital anemia of the newborn together with a comprehensive bibliography will be found in: *Diamond, L. K., Blackfan, K. D., and Baty, J. M.*: *J. Pediat.* 1: 267, 1932. (3) Additional references on congenital anemia of the newborn appearing since then and reviewed for this paper include: *McNeil, C.*: *Edinburgh M. J. (Tr. Med. Chir. Soc.)* 37: 175, 1930. *Pritchard, E., and Smith, J.*: *Arch. Dis. Child.* 6: 325, 1931. *Dalldorf, G., and Russell, H. K.*: *N. Y. J. Med.* 32: 839, 1932. *Happ, W. M.*: *J. Pediat.* 1: 638, 1932. *Segar, L. H., and Stoeffler, W.*: *J. Pediat.* 1: 485, 1932. *Akerren, Y.*: *Acta Pediat.* 14: 142, 1932. *DeLange, C.*: *Rev. franç. de pédiat.* 8: 448, 1932. *Bonar, B. E., and Smith, E. H.*: *Am. J. Dis. Child.* 45: 594, 1933. *Parsons, L. G., Hawksley, J. C., and Gittins, R.*: *Arch. Dis. Childhood* 8: 159, 1933. *Abt, A. F.*: *J. Pediat.* 3: 7, 1933. *Schwartz, A. B.*: *Wisconsin M. J.* 33: 98, 1934. *Pasachoff, H. D., and Wilson, L.*: *Am. J. Dis. Child.* To be published.

A SIMPLE ETHER OIL APPARATUS

R. P. LITTLE, M.D., SANTA PAULA, CALIF.

AN EFFICIENT apparatus for the administration of ether oil per rectum can easily and cheaply be assembled using a Mallineckrodt



ether can as a reservoir and a Becton, Dickinson & Co., stopcock and adapters. A tinsmith can do the soldering necessary in a few minutes.

TRACTION IN FORCEPS DELIVERIES

BURDETT WYLIE, B.S., M.D., CLEVELAND, OHIO

(From the Department of Obstetrics and Gynecology, Medical School, Western Reserve University.)

ONE finds discussed in the obstetric literature practically every phase of the use of forceps. The present study was conceived with the idea of determining just how much force must be applied to the forceps in the average case, in order to complete a delivery, and also what effect, if any, certain factors such as parity, color, age, etc., would have on the findings. The data were collected from cases on the Obstetrical Service at Cleveland City Hospital during the year beginning July 1, 1932.

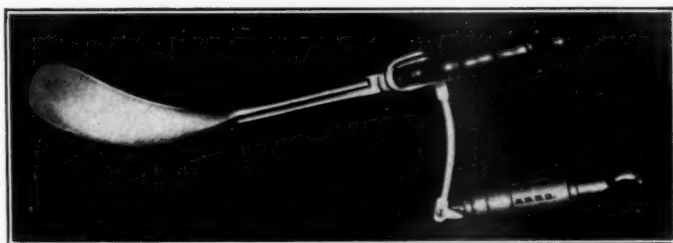


Fig. 1.—The Bill axis traction handle with traction recording modification (tractionometer) in place on Tucker-McLane blades. Traction applied in the direction of the pointer is measured and recorded by a ring which slides over a scale on the side of the mechanism.

The instrument used was a Bill axis traction handle in which a spring mechanism had been inserted, and Tucker-McLane forceps. This set-up insured an accurate application of force in the axis of the birth canal and minimized the resistance offered to delivery by the forceps themselves. The forceps were applied and observations obtained when the head had reached the pelvic floor, or in other cases where the head was engaged, and full dilatation of the cervix had taken place, but where there was undue delay in advancement. Obviously this routine offered an excellent opportunity for a study of this nature since the majority of patients presented no dystocia and, therefore, the findings represent for the most part the normal resistance encountered by the presenting part in the completion of the second stage of labor.

To further facilitate delivery the procedure of "ironing-out" the birth canal was used, employing a lubricating soap freely during this process. With the vagina and perineum well dilated and lubricated,

an accurate cephalic application of the forceps was then made. Traction, however, was not exerted until, by abdominal palpation, a uterine contraction was detected. The blades were then locked, the claw of the handle slipped into place and traction applied. This force was exerted only for the duration of the uterine contraction and an effort was made never to exceed the least amount of traction needed to advance the head. At the end of the contraction the head was allowed to slip back into the hollow of the sacrum, the handle removed, and the blades opened. At this time the maximum traction exerted during the preceding pull was read from the scale, and the recording ring of the instrument returned to zero. This procedure was then repeated during as many contractions as were necessary, until the head came down under the symphysis far enough to be grasped through a "chin towel." The blades were then removed and the completion of the delivery over the perineum done by hand.

During the period of this study 1,521 patients were delivered. In 1,068 (69.5 per cent) of these, forceps were used. Traction observations were made on 880 cases from this group. These were unselected with the exception of 13 cases that required the use of Tarnier blades, and hence could not be included in this series.

The data collected, as already stated, consisted of a series of figures representing the maximum traction, in kilograms, recorded in each pull of a series of pulls necessary to complete the second stage. There was the most extreme variation encountered between individual cases, not only in amount, but also in the number of pulls required. For example, among the primiparas the range was from a single pull of 5 kilograms to a series such as: 15-14-18-19-21-23-21-21-13-12 or in another case 26-27-27-30-29-28-23-12. Among the multiparas there were 64 patients delivered by single pulls of less than 5 kg., but here too the higher figures were sometimes reached, as in a case delivered by pulls of 20-24-25-25-27-27-33. The maximum traction recorded in any single pull was 34 kg. (74.8 pounds). The maximum number of pulls in any single case was 10.

It is obvious then, that, with such extreme variations from case to case, deductions to be of any value must be based on averages from a fairly large series of cases. With this in mind we have calculated our results in the various groups on the basis of, first, the average individual pull, and second, the average number of pulls. The force of the individual pull is, of course, the important factor so far as trauma to the mother or baby is concerned but, in order to get a true picture of the difficulty encountered in any particular case or class of cases, the number of such pulls needed to complete the delivery is also important. So, in calculating our results we have taken the product of the average individual pull times the average number of pulls in any series of cases, as the index of resistance encountered in that group.

This "Resistance Index" we believe, gives a fair estimate of the relative difficulty encountered on various groups of patients.

Employing the methods just discussed, the cases were studied according to various factors which it was thought might have a bearing on the ease or difficulty of delivery.

PARITY

The number of babies previously borne by a mother should be an important factor. Study of our data gave results as shown in Table I.

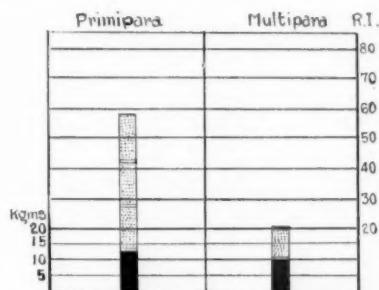


Fig. 2.—Graph showing the relative resistance found in primiparas and multiparas. Data from Table I. Key: Blocks represent the average individual pull, in kilograms. The number of blocks corresponds with the average number of pulls for the group. The resulting column represents the resistance index of the group.

It is immediately obvious that the greatest difference lies between the primipara and the multipara. In the latter group the para ii's are definitely higher than any of the others; above para v there appears to be a tendency to increasing resistance with higher parity.

On direct comparison of the multipara and primipara averages, we find that the resistance index has a relationship of 1 to 2.7. On the other hand, when the average individual pull is compared the relationship is only 1 to 1.4. This difference is compensated for by the increased number of pulls used in the primiparous cases. As has already been mentioned, it is reasonable to assume that injury, if any, will be the result of the more forceful pulls; it would seem logical, therefore, to keep the

TABLE I. PARITY

GROUP	CASES	AVERAGE PULL	AV. NO. PULLS	RESISTANCE INDEX
Primiparas	321	15.45 Kg. (34.0 pounds)	3.7	57.2
Multiparas	559	11.15 Kg. (24.5 pounds)	1.9	21.2
Para ii	244	11.97 Kg. (26.3 pounds)	2.1	25.1
iii	122	9.87 Kg. (21.7 pounds)	1.6	15.8
iv	76	9.68 Kg. (21.3 pounds)	1.7	16.5
v	34	10.25 Kg. (22.6 pounds)	1.5	15.4
vi	32	10.45 Kg. (23.0 pounds)	1.7	17.8
Over vi	51	11.15 Kg. (24.5 pounds)	1.8	20.1

maximum pull as low as possible and encourage a distribution of the energy over an increasing number of pulls as the delivery becomes more difficult. This policy was carried out as far as possible in the present study. It would be purely speculative but interesting to imagine what the results would have been, both as to force exerted and also on our morbidity and mortality data, had each delivery been com-

pleted by a single adequately forceful pull. Certainly, since the resistance encountered would have remained the same in each instance, the maximum effort exerted would have reached much higher levels which one would expect to see reflected in the end-results.

Another factor that should be repeated and emphasized is that traction was only applied during a period of uterine contraction, and was seldom sustained for more than about thirty seconds. In this way the damage was minimized which might be expected to follow prolonged compression of the fetal head and maternal soft parts. This policy also utilizes the expulsive force contributed by the contracting uterus. This is of unknown, and probably quite variable amount, but we feel assured that it was of real value in reducing the traction necessary in the average case.

Since such characteristic differences exist between primipara and multipara averages, we have calculated all our data under these two subdivisions.

Color.—Observations as to color offer variations that are of at least academic interest and lend some support to the popular impression that colored women have easier deliveries than white.

TABLE II. COLOR

	CASES	AVERAGE PULL	NO. PULLS	R. I.
Primiparas, white	236	15.95 Kg. (35.0 pounds)	3.9	62.2
Primiparas, colored	85	15.03 Kg. (33.1 pounds)	3.3	49.7
Multiparas, white	441	11.33 Kg. (24.9 pounds)	1.9	21.5
Multiparas, colored	118	10.37 Kg. (22.8 pounds)	1.7	17.6

Age.—The study according to age was not very satisfactory among the primiparas, since our cases for the most part fell in the groups between sixteen and thirty years. There were only 17 scattered cases outside this range, obviously not enough to consider. Within this limited range, however, there did appear to be a definite relation between age and traction, and it is possible that in a larger series this trend would have been seen to continue in the higher age groups.

TABLE III. AGE

PRIMIPARAS	CASES	AVERAGE PULL	NO. PULLS	RESISTANCE INDEX
16-20	176	14.84 Kg. (32.6 pounds)	3.5	51.9
21-25	96	15.96 Kg. (35.1 pounds)	3.9	62.2
26-30	32	16.7 Kg. (36.7 pounds)	4.6	71.8

Among the multiparas no significant age variation was discovered.

Position.—Observations according to position of the presenting part confirmed to a degree the expected influence of anterior and posterior presentation. The cases

TABLE IV. POSITION

	CASES	AVERAGE PULL	NO. PULLS	RESISTANCE INDEX
Primiparas Ant.	240	14.8 Kg. (32.6 pounds)	3.6	53.3
Primiparas Trans.	23	15.35 Kg. (33.8 pounds)	3.5	53.7
Primiparas Post.	55	17.9 Kg. (39.4 pounds)	4.3	77.0
Multiparas Ant.	484	11.06 Kg. (24.3 pounds)	1.8	19.9
Multiparas Trans.	18	9.69 Kg. (21.3 pounds)	1.4	13.6
Multiparas Post.	55	11.47 Kg. (25.2 pounds)	1.9	21.7

which had engaged and remained posteriors required slightly more effort to deliver, even though they had all been converted into anteriors by means of the Modified Seanzoni maneuver, before any traction was applied. These differences can reasonably be attributed to lack of molding. However, the differences are surprisingly small and would tend to indicate that while molding is of unquestioned importance in some cases, it is not of great significance in the average posterior case. We find a moderate increase of traction in the primiparas, posterior class, but among the multiparas this difference is negligible.

The figures for the transverse presentation are unexpectedly low, but since they are based on such a small group of cases we prefer to attach no particular importance or interpretation to them.

Type of Forceps Application.—When the cases are studied on the basis of type of forceps application, a more definite and important trend is demonstrated. Our series did not include any high applications and only ten high-midforceps, certainly not

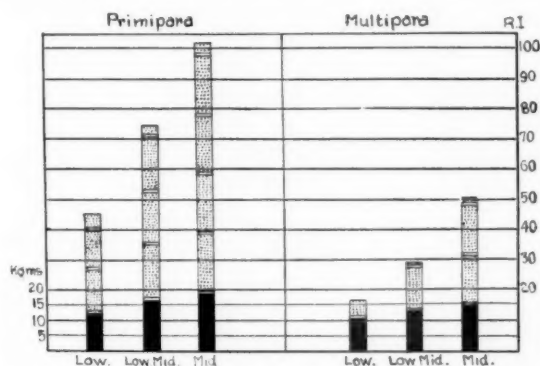


Fig. 3.—Graph showing relative resistance encountered, depending upon the type of forceps application. Data from Table V. (Key as in Fig. 2.)

enough to be significant. In the low, low-mid, and mid groups, however, the results were more definite and illustrate clearly the increasing difficulty one may expect to encounter when the head fails to descend after a moderate trial of second stage labor.

TABLE V. TYPE OF FORCEPS APPLICATION

	CASES	AVERAGE PULL	NO. PULLS	RE-SISTANCE INDEX
Primiparas, low	192	13.7 Kg. (30.1 pounds)	3.3	45.2
Primiparas, low-mid.	106	17.4 Kg. (38.3 pounds)	4.3	74.8
Primiparas, mid	15	19.31 Kg. (42.5 pounds)	5.3	102.3
Multiparas, low	434	10.03 Kg. (22.1 pounds)	1.7	17.1
Multiparas, low-mid.	101	13.3 Kg. (29.3 pounds)	2.2	29.3
Multiparas, mid	16	15.77 Kg. (34.7 pounds)	3.2	50.5

Trauma to Birth Canal.—Further study of the data demonstrated an interesting association between trauma and traction whereby the degree of trauma and the force exerted increased together. This is observed in both the primipara and multipara groups. The most logical explanation would seem to be that both trauma and increased resistance are brought about by either a relatively larger baby or by less elastic maternal tissues, or both.

Episiotomy in our series was performed only when a severe second-degree or third-degree laceration seemed inevitable. This group, therefore, properly follows the second-degree group in degree of trauma. There were no third-degree tears.

The data presented relative to cervical tears is interesting but somewhat distorted, not only due to the small number of cases but also due to the fact that the cervix was only inspected following a difficult labor or delivery that suggested probable damage at this site.

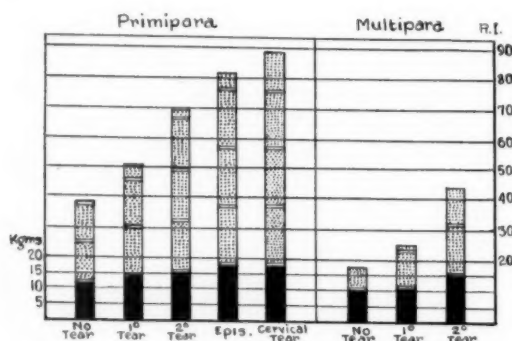


Fig. 4.—Graph showing the relative resistance encountered in groups arranged according to the degree of trauma to the birth canal. Data from Table VI. (Key as in Fig. 2.)

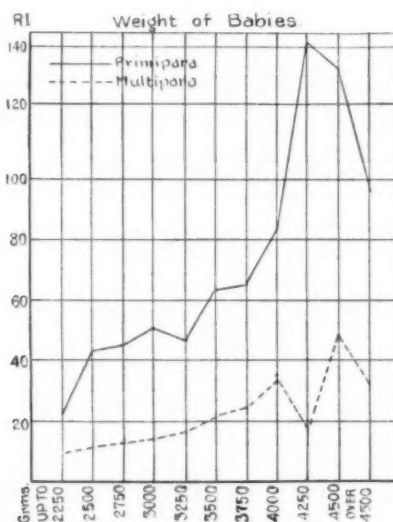


Fig. 5.—Graphs showing the relative resistance encountered in groups arranged according to the weight of the babies. Points plotted represent the resistance index for each weight group.

Weight of Babies.—The size of the baby is, of course, an important factor in determining the ease or difficulty of delivery. In Fig. 5 the weight of the babies has been plotted against the resistance index in the various size groups. Unfortunately, there were too few cases in some of the groups to give a true average, with a corresponding smooth curve, but the trend is quite obviously that of increasing resistance with increasing size of the baby. This is true in both the primiparous and multiparous groups.

TABLE VI. TRAUMA

	CASES	AVERAGE PULL	NO. PULLS	RE-SISTANCE INDEX
Primiparas, no tears	81	12.25 Kg. (27.0 pounds)	3.1	38.0
Primiparas, 1° tears	95	14.48 Kg. (31.9 pounds)	3.5	50.7
Primiparas, 2° tears	102	17.0 Kg. (37.4 pounds)	4.1	69.7
Primiparas, episiotomy	28	18.02 Kg. (39.6 pounds)	4.6	82.9
Primiparas, cervical T.	16	18.7 Kg. (41.1 pounds)	4.7	87.9
Multiparas, no tears	452	10.06 Kg. (22.1 pounds)	1.8	18.1
Multiparas, 1° tears	78	12.16 Kg. (26.8 pounds)	2.1	25.5
Multiparas, 2° tears	26	15.38 Kg. (33.8 pounds)	2.8	43.1

From the data so far presented an interesting correlation was observed between the size of the baby and certain other factors. From the data on primiparas we get the figures shown in Table VII.

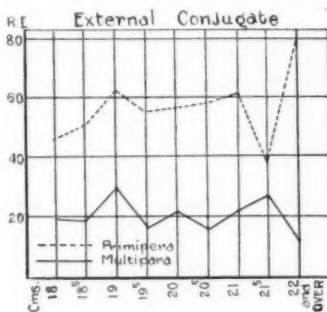


Fig. 6.

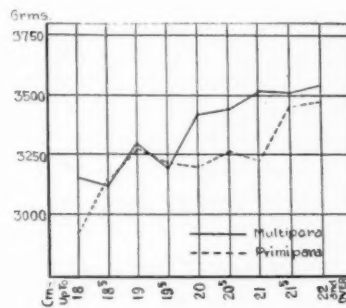


Fig. 7.

Fig. 6.—Graph showing the relative resistance encountered in groups arranged according to the measurement of the external conjugate. Points plotted represent the resistance index for each size group.

Fig. 7.—Graph showing the average weight of babies in groups arranged according to the measurement of the external conjugate.

While there are many interacting factors which make the problem too complex for complete analysis, we feel that probably in the majority of cases a relatively large baby is the primary cause of not only the higher forceps application, but also of the increased resistance and trauma as well, rather than that any of these factors bear a direct cause and effect relationship to each other.

TABLE VII

	RESISTANCE INDEX	TEARS OF ALL DEGREES	AVERAGE WT. OF BABIES
Low forceps	45.2	65.6%	3,133 gm.
Low-midforceps	74.8	84.0%	3,264 gm.
Midforceps	102.3	100.0%	3,304 gm.

Size of Pelvis (External Conjugate).—The size of the pelvis, as expressed by the external conjugate would also seem to be a good index of the probable resistance to be encountered at delivery. This impression, however, is not borne out. Among the multiparas the traction needed for delivery remained practically the same regardless of this measurement, while among the primiparas, there was an actual tendency for deliveries to become more difficult as the external conjugate became larger.

The answer to this is obvious when the weight of babies is plotted against the size of the pelvis (Fig. 7), it then becomes apparent that any advantage gained by the larger pelvic measurement is lost due to increased size of babies in these cases.

Morbidity and Mortality.—There were 14 mothers (1.6 per cent) who developed serious complications such as phlebitis, metritis, etc., following delivery. These might be attributed to trauma; however, the actual traction was found to be well below the average in these cases. Two mothers were lost, both from septicemia (2.2 per 1,000). One, a primipara, was delivered by traction moderately in excess of the average. The other, a multipara was delivered by traction far below the average.

Considering the infant mortality, there were 31 stillbirths and neonatal deaths, giving a gross mortality of 3.4 per cent. The causes of death were diagnosed as follows: Prematurity, 9; macerated stillbirth, 2; pneumonia, 5; hemorrhagic disease of N. B., 1; premature separation of placenta, 2; infection, 1; congenital deformity, 2; asphyxia neonatorum, 9. Autopsies were performed on 26 or 84 per cent of these. In none was cerebral hemorrhage found. Two of the babies diagnosed as asphyxia neonatorum were not posted, however; they had presented no clinical evidence suggestive of cerebral injury and the traction exerted had been far below the average in each case. Three of the asphyxia neonatorum cases had been subjected to traction slightly above the average. In the remaining six, traction was far below the average.

Thus we feel justified in not considering trauma as an important factor in our morbidity and mortality record.

CONCLUSIONS

The data just presented have been prepared with the idea of making certain academic observations on the amount of force involved in routine forceps work. For this reason the exact methods employed have been described in some detail, since comparisons and interpretations can only be made with these details in mind. It should also be pointed out that in routine work it is very difficult to set up any satisfactory division in the records between "prophylactic" or elective forceps and truly operative causes. For this reason the averages presented here include many cases which would have been operative cases in the hands of the most conservative. In addition, some of the persistent occiput posteriors handled in this series by the Modified Scanlon maneuver and forceps extraction, would in other clinics be delivered in some other way. It is, therefore, obvious that our averages are somewhat above those which one would obtain from truly normal "elective forceps" cases, but they do represent routine forceps findings.

The question of what relationship exists between these traction figures and the force which the patient herself would have to exert delivering the same baby spontaneously, is one which does not permit of any but a speculative answer. The traction figures represent an equivalent amount of resistance to delivery. This resistance would remain practically the same to spontaneous delivery; thus the amount of spontaneous effort required would at least be proportional, if not equal, to that actually recorded.

Our own opinion is that if it were possible to measure spontaneous effort, there would be found a fairly close correspondence between the force exerted in a spontaneous expulsion and the figures presented here, with the exception that the forceps extraction, being mechanically more efficient, would reduce the effort required to a moderate extent in this form of delivery. In the posterior cases, however, we believe the effort required to complete delivery following a Modified Scanzoni is only a fraction of that which the mother would have to exert in order to rotate the head and deliver the same baby herself.

As for the use of the tractionometer, we found it of great value as an aid in teaching new men. It was observed that men with considerable experience had no idea how hard they pulled in terms of pounds or kilograms. It was, therefore, impossible to tell a beginner how hard to pull or to know how hard he was pulling during a delivery. Using this appliance, however, it is possible to suggest the probable traction required and at all times to know just how much force is being exerted and to alter this as occasion arises. To the experienced operator himself, traction readings act as a definite incentive for increased gentleness and accuracy in forceps work.

Finally, the inclusion of these readings in the case history gives a direct record of just how difficult the delivery was, and will be a very valuable addition to the hospital files in the event of any follow-up studies on these mothers or babies at some later date.

Fleurent, Keller, and Meyer: Chorionepithelioma of the Tube, *Bull. Soc. d'obst. et de gynec.* 5: 452, 1933.

There are 32 cases of chorionepithelioma of the fallopian tube reported in the literature. Compared with the frequency of extrauterine gestation, chorionepithelioma of the tube is not less frequent than the same affliction of the uterus after uterine pregnancies. In most of the 32 cases reported, the women had had from one to five pregnancies while a few had never before been pregnant.

The diagnosis of chorionepithelioma of the tube presented serious difficulties but the diagnosis was suggested by the following clinical facts: A history of extrauterine pregnancy; an intervening period of a few weeks or months; reappearance of bleeding accompanied by abdominal pain; an adnexal tumor which was growing rapidly; metastases on the vulva or in the vagina; an empty uterine cavity; cachexia and pronounced anemia and the formation of metastases in the body.

The prognosis was grave. Among the 32 cases there were only three recoveries. Treatment consisted not only of removal of the tube containing the tumor and the visible metastases but also of a complete hysterectomy. This was to be followed by roentgen ray applications.

J. P. GREENHILL.

EXPERIMENTAL STUDIES OF PUERPERAL INFECTION

V. THE VARIATION IN THE SUSCEPTIBILITY OF THE SKIN TO STREPTOCOCCUS TOXIN DURING PREGNANCY

CALVIN C. TORRANCE, M.D., ALBANY, N. Y.

(From the Division of Laboratories and Research, New York State Department of Health)

AN EXPERIMENTAL study of puerperal infection was undertaken to determine whether susceptibility to the invasion of micro-organisms was altered at the time of pregnancy. Our early studies indicated that pregnant mice were more susceptible to infection with hemolytic streptococci inoculated intraperitoneally than were non-pregnant mice. Subsequent studies^{1, 2} on the survival of pathogenic bacteria in the vagina, on hemolytic complement, and on the production of agglutinating activity in the serum have failed to reveal any significant immunologic difference between pregnant and virgin rabbits.

Two authors have reported an unusual response to intradermal injections of streptococcus toxin during pregnancy. Weiss³ tested the reactivity of the skin to this toxin at frequent intervals in a group of pregnant women. Eleven of the patients whose skin reacted to the toxin early in pregnancy failed to show this reaction following delivery. On the other hand, nine patients in whom the tests had been negative originally reacted later on. In another twenty-seven patients, the reaction, while not completely reversing itself, varied in its intensity, becoming either weaker or stronger. Burton and Balmain⁴ tested 221 pregnant women and separated 36 with positive reactions from the main group for retesting, which was done at monthly intervals. Sixteen of the women had negative reactions before delivery, but in three patients the reaction reverted to positive at a later date.

Observations made in this laboratory, where goats and rabbits are used in the standardization of toxin, indicate that the skin of these animals also may become insensitive to toxin when they are pregnant. They were, therefore, considered to be suitable for use in a more detailed investigation of this problem.

METHOD OF INVESTIGATION

Chinchilla rabbits were chosen for the experiments since in these animals the reaction of the skin to streptococcal toxin is similar to that of the human skin. Those selected were too young to have been pregnant and were isolated for at least a month before use. The toxin employed was produced in this laboratory by the Dochez N. Y. 5 strain of the *Streptococcus hemolyticus*, originally obtained from a case of scarlet fever. Toxin, heated in a boiling water-bath for two hours, and uninoculated toxin broth were used as controls to eliminate reactions which were not due to the toxic principle itself. Each rabbit received five injections: first,

a 1:1,000 dilution of broth; second, a 1:1,000 dilution of heated toxin; third, fourth, and fifth, 1:4,000, 1:2,000, and 1:1,000 dilutions of toxin (one, two, and four skin-test doses). The diluted materials were injected intracutaneously in 0.1 c.c. amounts into the animal's back after it had been denuded of hair.

The tests were read and recorded at the end of twenty-four and forty-eight hours. If the two readings did not agree, the stronger was recorded as the final result. The degree of reaction was expressed thus:

If the injection of 1 S.T.D. was followed by a reaction 10 mm. in diameter or greater	3+
If 2 S.T.D. caused a reaction greater than 10 mm., while the 1 S.T.D. was less than 10 mm.	2+
If the toxin contained in 4 S.T.D. caused a reddened area at least 10 mm. in diameter, while the 1 or 2 S.T.D. was less	+
If all the injections resulted in a visible reaction but of less than 10 mm. in diameter	±
No reaction	-

First Experiment.—Twelve female rabbits were tested for skin sensitivity to streptococcal toxin at weekly intervals for nine weeks. The animals were subdivided into six groups of two animals each.

Group 1: Rabbits were neither immunized nor mated. While the skin of one (No. 6836) did not react to the weaker dilutions of toxin during the preliminary tests, as is frequently the case with young rabbits, it became more sensitive as the experiment progressed, and after attaining 3+ continued to give that reaction throughout the remainder of the period of observation. There was no change in the skin sensitivity of the other rabbit (No. 6843).

Group 2: Preliminary skin tests repeatedly gave 3+ reactions. The rabbits were then mated. Their skin reacted only to the higher concentrations of toxin during the latter part of the gestation period (see Table I). One animal failed to react to the 4 S.T.D. injection of toxin just before, and the other after, delivery. In the last test, made two weeks after delivery, the skin of both animals was still insensitive.

Group 3: Rabbits were immunized but not mated. After the preliminary test and at about the time the other animals were mated, the following series of subcutaneous injections of toxin was given: after an initial 4,000 S.T.D., the dose was doubled every five or six days until the fifth and last injection of 64,000 S.T.D., which was made just before the young were born. Rabbit 6839 died after the first injection of toxin and before another skin test had been done. *B. dysenteriae* Flexner was recovered from the heart's blood and was probably responsible for the death of the animal. The other rabbit (No. 6888) reacted to the smallest amount of toxin after the first two immunizing injections; after two more, 16,000 and 32,000 S.T.D., respectively, the reaction became ±; the skin failed to react to any toxin dilution after the final dose of 64,000 S.T.D.

Group 4: Rabbits were mated. They were then immunized with the same doses as Group 3 animals received. The skin reaction of Group 4 rabbits began to change sooner than did that of the nonpregnant immunized animal (see Table I).

Groups 5 and 6: Rabbits of the former group were not mated; those of the latter were. All received an intravenous dose of 0.25 c.c. of an eighteen-hour broth culture of living streptococci shortly after animals of the sixth group were mated. Unfortunately, three rabbits developed septicemia as a result of this treatment and

TABLE I. SKIN TEST FOR SUSCEPTIBILITY TO STREPTOCOCCUS TOXIN
Comparison of Reactions in Rabbits Before, During, and After Pregnancy, With Virgin Animals

ANIMAL NUMBER	METHOD OF IMMUNIZA- TION	SKIN REACTION						REMARKS
		BEFORE* PREGNANCY	DURING PREGNANCY				POST- PARTUM†	
			FIRST WEEK	SECOND WEEK	THIRD WEEK	FOURTH WEEK		
Group 2		3+	3+	3+	3+	2+	-	Died following inoculation with living culture. Microscopic evidence of pregnancy. Killed to determine pregnancy. 8 dead fetuses in uterus.
6889		3+	3+	3+	±	-	-	
6846								
Group 4		3+	3+	3+	+	-	-	
6834	Toxin	3+	3+	2+	+	-	-	
6893	Toxin	3+	3+	2+	+	-	-	
Group 6		3+	-	-	D			
6856	Culture							
6847	Culture	3+	2+	3+	±	-	D	
Unmated Control Groups								
Group 1		+	3+	3+	3+	3+	3+	Died of intercurrent infection. Died following inoculation with living culture. Died following inoculation with living culture.
6836		3+	3+	3+	3+	3+	3+	
6843								
Group 3		3+	2+	3+	3+	±	-	
6888	Toxin	3+	3+	D				
6839	Toxin	3+	3+					
Group 5		3+	3+	-	D			
6852	Culture							
6886	Culture	3+	-	-	D			

*Average of three readings.

†Final testing two weeks after delivery.

died. While the skin reaction in all three changed, and none was elicited in the final test, it is doubtful whether any significance can be attached to these results, since the animals were moribund at the time. Rabbit 6847, one of the animals that had been mated, recovered from the inoculation. The skin of this animal became insensitive during the last week of the gestation period. She failed to deliver her young at the expected time, however, but, when she was killed, an autopsy revealed eight partially absorbed fetuses in the uterus.

Second Experiment.—At the termination of this experiment a second was begun. This not only served to confirm the results of the first but provided material for passive transfer and for other experiments which will be discussed later.

Five pregnant and seven nonpregnant rabbits were given skin tests at weekly intervals (see Table II). The skins of three of the five failed to react to any toxin dosage at or about the time of delivery. Only minor fluctuations were noticed in the reactions of the other two pregnant rabbits and the virgin controls.

TABLE II. SKIN TEST FOR SUSCEPTIBILITY TO STREPTOCOCCUS TOXIN
Comparison of Reactions in Rabbits Before, During, and After Pregnancy

ANIMAL NUMBER	SKIN REACTION							
	BEFORE* PREG- NANCY	DURING PREGNANCY				DE- LIVERY	POSTPARTUM	
		FIRST WEEK	SECOND WEEK	THIRD WEEK	FOURTH WEEK		FIRST WEEK	SECOND WEEK
2006	3+	3+	3+	2+	3+	3+	2+	3+
2009	3+	3+	3+	3+	3+	3+	3+	3+
2008	3+	3+	3+	+	3+	—	2+	D
2010	3+	3+	2+	3+	3+	2+	—	3+
2012	3+	2+	+	**	3+	—	—	3+

Pregnancy With Virgin Animals

2001	3+	3+	2+	±†	3+	3+	3+‡	3+
2005	3+	3+	3+	3+	3+	3+	3+	3+
2007	3+	**	3+	3+	3+	3+	3+	3+
2013	3+	3+	3+	3+	3+	3+	2+	3+
2002	3+	2+	3+	2+	3+	3+	3+	**
2003	3+	2+	3+	3+	3+	3+	3+	3+
2004	3+	2+	3+	3+	3+	3+	3+	3+

*Average of four readings.

**Test impossible or unsatisfactory because of pigmentation of the skin.

†Reaction may have been due to position of test low on the animal's side.

‡Heated control induced a reaction nearly equal to the 1 S.T.D. of toxin.

Testing Serum for Antitoxin.—At this time, the three rabbits with insensitive skins were bled from the heart; the serum was separated from the clot aseptically and made up with varying amounts of physiologic salt solution and toxin to determine whether any detectable amount of antitoxin was present. Injection of the mixtures into the back of a sensitive rabbit demonstrated that no neutralization of the toxin had taken place. By the methods employed, amounts less than 0.2 of a unit of antitoxin per cubic centimeter of serum could not be detected.

Passive Transfer of Serum.—When no antitoxin could be demonstrated in the serum of the insensitive rabbits, 3 c.c. of serum from one was injected into a tattooed area in the back of a sensitive rabbit. Twenty-four hours later, toxin was injected into the center of this prepared area and also into a normal area outside it. Both toxin injections induced the customary reactions. A second sensitive rabbit was then prepared, with three tattooed areas on its back. One cubic centimeter of serum from an insensitive rabbit was infiltrated into the skin of the first area. Twenty-four hours later the second area and twelve hours later the third tattooed

region were similarly treated. Finally, twelve hours after the last injection of serum, toxin was injected into the center of each prepared area and into a suitable area of skin outside of them. None of these toxin injections induced reactions. When the experiment was repeated on a second sensitive rabbit with the serum from a different insensitive pregnant rabbit, the results were the same, except that the control toxin injection outside of the prepared areas showed a very slight reaction at the twenty-four-, but none at the forty-eight-hour reading.

To control these results, the experiment was repeated with the injection of normal serum from a sensitive rabbit in one animal and, in another, serum from an immunized nonpregnant rabbit with an insensitive skin. These serum injections did not influence the skin reactions in any way.

Experiments With Follicular Hormone.—In an effort to elucidate this phenomenon further, pseudopregnancy was induced in two rabbits by giving them gradually increasing doses of follicular hormone. After the first course of injections had been administered, the abdomen of each rabbit was opened under ether anesthesia; one horn of the uterus was removed for histologic examination, and nonabsorbable sutures were placed in the other.

The administration of the hormone was repeated every third or fourth day. The reaction of the skin to intradermal injections of toxin was determined after each dose of hormone had been given. Despite the fact that both rabbits built nests and had decidual reactions in the uterus, no alterations in the reactivity of the skin occurred.

DISCUSSION

Kunz and Nobel⁵ and Burt-White and others^{6, 7} have advocated the use of intracutaneous tests with streptococcal toxin to determine the susceptibility of pregnant women to puerperal infection. They believe that concentrated efforts can then be made to protect those who react to the toxin. While the experiments reported in this paper have not demonstrated the mechanism of the peculiar insensitivity of the skin late in pregnancy, they do indicate that intradermal tests with streptococcal toxin in gravid animals are no measure of specific immunity to this substance. They further indicate that, unless the refractory state of the skin also represents a nonspecific decrease in susceptibility to infection with the streptococcus in other tissues of the body, skin tests performed during pregnancy reveal no information of value concerning the possibilities of later infection with this microorganism. Numerous observations^{3, 8, 9, 10, 11} on human subjects have failed to indicate that the insensitive state of the skin which occurs in some pregnancies denotes a lessened susceptibility to streptococcal infection.

SUMMARY AND CONCLUSIONS

Seven nonimmunized rabbits were tested for susceptibility to streptococcal toxin at weekly intervals during pregnancy. In five of these animals the skin failed to react to intradermal injections of toxin at or about the time of delivery. Antitoxin was not found in the blood, to account for this change in skin sensitivity. On the other hand, the serum of pregnant rabbits did desensitize the skin of a normally

sensitive animal when it was injected forty-eight hours before the test was performed. While these changes occurred with natural pregnancy, they were not duplicated in pseudopregnancy.

The results of this study thus suggest that some factor, or factors, other than antitoxin or the follicular hormone is responsible for the loss of reactivity to streptococcal toxin that occurs in the skin during pregnancy.

REFERENCES

- (1) *Torrance, C. C.*: AM. J. OBST. & GYNEC. 27: 863, 868, 1934. (2) *Torrance, C. C.*: J. Immunol. 27: 531, 1934. (3) *von Weiss, H.*: Zentralbl. f. Gynäk. 51: 2330, 1927. (4) *Burton, A. H. G., and Balmain, A. R.*: Lancet 218: 1063, 1930. (5) *Kunz, H., and Nobel, E.*: Ztschr. f. Kinderh. 42: 372, 1926. (6) *Burt-White, Harold*: Brit. M. J. 1: 974, 1928. (7) *Burt-White, Harold and others*: Brit. M. J. 1: 240, 1930. (8) *Salmond, Margaret, and Turner, Beatrice*: Brit. M. J. 2: 145, 1929. (9) *Stent, Lois*: Lancet 218: 1066, 1930. (10) *Hudson, G. E.*: Illinois M. J. 60: 328, 1931. (11) *Baird, Dugald, and Cruickshank, Robert*: Lancet 219: 1009, 1930.

TRAUMATIC RUPTURE OF AN EARLY PREGNANT UTERUS

G. S. REEDER, M.D., AND C. G. MOORE, M.D., FREMONT, NEB.

MRS. F., aged nineteen, para ii, weight 90 pounds. Menstruation normal, twenty-eight-day type. Normal delivery December, 1932. The last menstrual period on Feb. 1, 1934.

The evening of June 6, 1934, Dr. G. S. Reeder found the patient suffering from intermittent pains at about five-minute intervals. There was a slight bloody, vaginal discharge. Patient was between four and five months pregnant. A diagnosis of threatened abortion was made, and morphine $\frac{1}{4}$ gr. administered. The following morning the patient was suffering from low abdominal pains at five-minute intervals with continuance of the vaginal discharge; pulse 110, rather weak; temperature 99°; expression anxious, the pains severe and directed to the back and into both thighs. On bimanual examination the uterus was found to be about the size of a four and one-half months' pregnancy, the cervix admitted one finger easily. The lower abdomen was distended. Patient gave evidence of shock which was interpreted as due to an internal hemorrhage; probably from a ruptured extrauterine pregnancy.

Patient was transferred to the Lutheran Hospital, Fremont, Nebraska, and an abdominal section performed by Dr. C. G. Moore, shortly after admission. At the time of operation the pulse was 116 but of fair volume; temperature 99.4°, respiration 22, Hb 37 per cent, R.B.C. 3,600,000.

The abdomen contained a moderate amount of free dark, clotted blood. The fetus had escaped into the peritoneal cavity, the placenta being in the posterior culdesac. The uterus was firmly contracted and presented a rent which extended the length of the body of the uterus on the left side. A supravaginal hysterectomy was performed, and the left ovary was removed. The patient made an uneventful recovery.

Comment.—No myomectomy and no cesarean section had been performed prior to this pregnancy. This case is unique in that the violence done the uterus was indirect and occurred in the early months of pregnancy. It is believed that this woman received a direct blow upon her side when riding on a merry-go-round, although she was not aware of it. It seems probable that the rupture did not occur until after uterine contractions had set in; that a myometrium, infiltrated with blood, predisposed the organ to rupture when labor pains came on.

PENTOBARBITAL SODIUM ANALGESIA*

WITH A REPORT OF 205 CASES

JAMES PHILIP BOYLAN, M.D., NEW YORK, N. Y.

(From the New York Nursery and Childs Hospital)

THIS report deals with a series of 205 cases in which pentobarbital sodium was used as an obstetric analgesic. At first nontoxic service cases were selected without prejudice, and later also trial labors and mild toxemias were included. Observations were made and recorded as "good," "fair," "poor," and "failures," in both objective and subjective results. No cases of what were thought to be excellent results were admitted; they were recorded as "good." Those of total failures will be discussed separately. "Good" was recorded when for objective results the patient was apparently unconscious, was cooperative, there was no delay of labor in any form, the third stage was satisfactory, and the baby did not require resuscitation. In good subjective results, the patient admitted, on questioning after delivery, a loss of pain sensibility, amounting in most cases to a total amnesia; "fair" was a somewhat lesser degree of the above; "poor" was recorded when the sum total of the effects obtained was so little better than a nonanalgesic labor that it was hardly worth while to have given the medication; "failures" were those in which there was no apparent effect from the drug.

Objective and subjective results were differentiated because we found that what was apparently a poor result objectively, in that the patient was mildly restless and complained of pain during her labor, was not a poor result subjectively, since on careful questioning later as to details, the patient had no recollection of the preceding hours. A patient who might have had a fair memory of her labor has been classified as a poor objective result, if there were a lack of cooperation, restlessness, or hemorrhage.

This investigation has demonstrated the value of satisfactory physical equipment and location of the labor room and the importance of a well-trained and cooperative nursing staff. It was observed that when patients were kept either completely or practically isolated, the results were better. It was found that those patients under the effects of the analgesic who had a minimum of external stimuli of all types, and who were spoken to or examined only when distinctly necessary (and these procedures of the utmost gentleness), had better results

*Read at the New York Academy of Medicine, Section of Obstetrics and Gynecology, April 24, 1934.

than those for whom these factors were not considered. In some cases we were frequently met with a language difficulty, and we believe that for the best results it is important to have the ends the obstetrician is attempting to obtain, explained to, and understood by the patient. A psychic appeal should be made for her cooperation.

TABLE I

		GOOD %	FAIR %	COM- BINED %	POOR %	FAILURE %	COM- BINED %
Pentobarbital 90 multiparas	Obj.	44.4	41.1	85.5	2.3	12.2	14.5
	Subj.	26.0	56.5	82.5	3.2	14.3	17.5
Pento-Scop. 38 multiparas	Obj.	63.2	23.6	86.8	5.2	8.0	13.2
	Subj.	50.0	33.3	83.3	6.7	10.0	16.7
Pentobarbital 37 primiparas	Obj.	46.0	25.9	71.9	11.9	16.2	28.1
	Subj.	40.8	37.0	77.8	7.4	14.8	22.2
Pento-Scop. 40 primiparas	Obj.	47.5	40.0	87.5	5.0	7.5	12.5
	Subj.	38.4	53.8	92.2	3.9	3.9	7.8

These criteria are not new or unknown, but are mentioned now since they are very often overlooked, and in not infrequent instances make for the success or failure of the procedure.

We have taken "good" and "fair" as satisfactory, and "poor" as unsatisfactory results.

The figures in Table I demonstrate that pentobarbital sodium when combined with scopolamine gave better results objectively and subjectively in both multipara and primipara.

Primiparous patients gave the poorest results and the largest percentage of failures when pentobarbital sodium alone was used, and the best results when it was combined with scopolamine.

It will be observed by referring to column 3 that multiparous patients were rated slightly better objectively than subjectively, whereas primiparous patients were the reverse, giving relatively better subjective than objective results.

It is interesting to note that although the percentage of satisfactory results objectively and subjectively in the individual groups differs as much as 5.9 per cent, the total percentage of satisfactory results for all cases was 83.6 objectively and 83.7 subjectively, a difference of 0.1 per cent.

Blood Loss.—Blood lost was measured, not estimated. The average loss for all cases was 190 c.c. There were seven instances in which the amount exceeded 500 c.c. Of these, six had a duration of labor of from thirteen to thirty-four hours, with an average of twenty-two hours. The seventh suffered a loss of 650 c.c. of blood following a three-hour labor, during which she had been given $4\frac{1}{2}$ gr. of pentobarbital sodium, and $\frac{1}{200}$ gr. of scopolamine. Check-up revealed that the fundus had been permitted to fill with blood. The greatest amount of blood lost in any case

was that of a patient's losing 900 c.c., following a labor of thirty-four hours with 6 gr. of pentobarbital sodium. At the time of delivery, she was markedly exhausted.

Time of Administration and Dosage.—Medication was instituted when the patients were well established in labor with three- to five-minute strong pains and at least a two-finger dilatation of the cervix. Varying doses, and intervals, as well as repetitions of the drugs, were given. At the beginning small doses of pentobarbital sodium alone were used, and later, minimum doses, repeated at half-hour intervals, were administered. Toward the end of the investigation, as more knowledge was obtained, and a greater security developed, and when apparently the most satisfactory results were obtained, we were using an initial dose of $4\frac{1}{2}$ gr. of pentobarbital sodium, with $\frac{1}{150}$ gr. of scopolamine, given simultaneously, and the dose, in whole or in part, repeated in approximately three to four hours. The minimum amount given was $1\frac{1}{2}$ gr. of pentobarbital sodium, and the maximum, 9 gr. of pentobarbital sodium, and $\frac{1}{100}$ gr. of scopolamine. No toxic effects were noted with this, our largest dose. It may be well to caution, however, that no arbitrary amount of the drug, or time interval can be established. Every case should be under careful observation at all times.

Failures.—There were twenty-three cases of failure. Fourteen were in multiparas and nine in primiparas. In twelve of the twenty-three, we attribute the failure to the medication's having been given too late in labor, with the maximum time of forty, and the minimum time of sixteen minutes before delivery. This was obviously too short a time for full effect of the drug. Vomiting of the capsules occurred three times. One patient was given the minimum dose, $1\frac{1}{2}$ gr. of pentobarbital sodium. Another had 3 gr. seven hours before delivery, the dose not repeated, and the effect had worn off when it was most needed. There were three instances of excitement. Besides these, there was a language difficulty with three other mothers.

We believe the last mentioned to be nonacceptable cases for analgesia because of the lack of psychic appeal.

There was no maternal mortality.

Babies.—There were 206 babies delivered in this series. Two hundred and one were living and breathed spontaneously. One set of premature, thirty-four-week twins required artificial resuscitation, but subsequently did well. Three babies were stillborn. The fetal heart of none of these was heard on admission of the mother to the hospital.

Contractions.—Contractions were found to be slowed in 4 per cent of the cases. The maximum time recorded was twenty minutes. Where a "fair" or "good" effect was obtained, it was noted that the uterine contractions continued at regular intervals and unabated strength.

Excitement.—Three cases of marked excitement were noted. We believe they could be physically controlled by intelligent handling on the part of the delivery room personnel. The application of delivery table accessories and administration of nitrous oxide oxygen were found to be sufficient. It has been recommended that an ampule ($7\frac{1}{2}$ gr.) of caffeine sodium benzoate, or apomorphine in subvomiting doses ($\frac{1}{40}$ to $\frac{1}{16}$ gr.), be given as an antidote. Neither was used in this investigation. Of the three cases of marked excitement, one was a patient who did not speak English, and who was very apprehensive. Another was a nervous West Indian negress of low mentality. The third was a syphilitic patient who had a macerated stillborn. We would not recommend giving pentobarbital sodium to these types of patients during a subsequent labor.

Blood Pressure.—Blood pressure readings recorded immediately before and one-half hour after administration of the analgesic, showed comparatively little change.

The maximum recorded change was 20 systolic and 15 diastolic, about equally divided between rise and fall. There was no case of shock.

Subsequent Anesthesia.—Final anesthesia was given in about 50 per cent of the cases by internes, and in the other half by the resident anesthetist of the hospital. She has reported all pentobarbital sodium cases as using less anesthetic than the others, and more than half of these, about 25 per cent of the total number of patients, needing little or no ether at the end of the second stage. Recovery immediately postpartum was found to be uneventful. There was no case of marked respiratory infection.

Operative Incidence for all ward deliveries at this hospital over the same period of time was 19.1 per cent. The operative incidence for this series was 16.1 per cent. Neither includes cesarean sections. This shows a slight lowering of the operative interference, following the exhibition of these drugs.

SUMMARY

There was no maternal mortality. There was no fetal mortality that could be attributable to the drug. Labor was not inhibited for any appreciable time, and delivery anesthetic was reduced. The third stage of labor was without untoward incident, and postpartum recovery was uneventful. Blood loss was within normal limits, and blood pressure was not appreciably affected. Excitement occurred infrequently and was controllable. The combination of pentobarbital sodium with scopolamine proved more effectual than the former alone.

CONCLUSIONS

1. Medication should be given early to be effective. The patient should be definitely in labor, the cervix thin, and one to one and one-half fingers dilated, and the dose repeated in whole or in part if necessary.
2. All external stimuli should be avoided.
3. The complete cooperation of a well-trained assisting staff is important.
4. This drug should be administered only to carefully selected patients.
5. Sufficient medication is necessary, and careful observation of the patient is essential.
6. The limits of the investigation have confirmed the original premise, i. e., safety for mother and child.

Vallebona, A., and Giavotto, G.: *Therapy with Short Wave Length Diathermy in Pelvic Inflammatory Disease in Women*, *Folia gynec-demograf.* 31: 207, 1934.

The authors used diathermy of 200 meters instead of the usual 500-600 meters diathermy wave lengths. In 30 cases they found inflammatory processes greatly benefited.

MARIO A. CASTALLO.

AN ANALYSIS OF MATERNAL MORTALITY IN TEN THOUSAND OBSTETRIC CASES

DAVID FEINER, M.D., F.A.C.S., BROOKLYN, N. Y.

(From the Obstetrical and Gynecological Service of the Israel Zion Hospital)

THIS presentation is a detailed study of the maternal mortality of 10,000 consecutive obstetric cases treated at the Israel Zion Hospital from 1923 to 1932. It is a portion of a comprehensive survey of a cross-section of obstetrics as observed and managed in a general hospital with a large visiting staff participating in the same. The purpose of this paper is not merely to review the mortality statistics of an obstetric service but to analyze each death as to whether or not it was preventable. Thus, an attempt is made to ascertain the factors responsible for the fatality and to point out in each instance what can be learned concerning the proper management of a similar case.

No paper of this type can possibly fail to call attention to the recently issued report of the New York Academy of Medicine Committee on Maternal Mortality.¹ Their appalling conclusion that 65.8 per cent of 2,041 maternal deaths were preventable should make us pause and take stock of our *modus operandi*. In this paper we report 36 maternal deaths, which is a rate of 3.6 per thousand, or 0.36 per cent. Of these, 17 occurred in primiparas and 19 in multiparas. Eight multiparas were para i, 5 were para ii, 3 were para iii, 2 were para iv, and 1 was para ix.

The method of delivery and operative procedures were as follows:

Undelivered	10	3 primiparas and 7 multiparas
Spontaneous deliveries	14	6 primiparas and 8 multiparas
Low forceps	2	1 primipara and 1 multipara
Midforceps		1 primipara
Incision of cervix and forceps		1 primipara
Two-forceps maneuver		1 primipara
Version and extraction		1 primipara
Version and craniotomy		1 primipara
Porro cesarean section		1 multipara
Classical cesarean section		1 primipara
Low cervical 2-flap section	3	2 primiparas and 1 multipara

The causes of death were as follows: Sepsis 10, hemorrhage 5, eclampsia 5, cardiac 4, pneumonia 3, embolus 3, ruptured uterus 2, preeclamptic toxemia 1, tuberculosis 1, diabetes 1, and spinal anesthesia 1.

AN ANALYSIS OF THE MATERNAL MORTALITY ACCORDING TO
OPERATIVE PROCEDURE

In 10,000 cases there was operative interference in 1,621, an incidence of 16.2 per cent. Operative procedure was done in only 12 of the 36 maternal deaths. If we may disregard causes of death and associated complications, in 1,621 instances of operative interference there were 12 fatalities or an incidence of 0.75 per cent. The operative procedures are as follows:

Forceps.—Low forceps constituted 75 per cent among 3,110 instrumental deliveries; the balance was midforceps, with the exception of 4 high forceps dating back to the beginning of this series, before this procedure was abandoned in favor of version or cesarean section. Uterine inertia and fetal distress were the indications for over half of the total number. Concerning the latter, a drop in rate and an irregularity in rhythm were considered of more significance than an increase in rate. Forceps delivery was necessary 3 times more frequently in primiparas than in multiparas. The gross fetal mortality incident to forceps delivery was 5 per cent, with the duration of labor obviously a potent factor in increasing the same. Routine episiotomy was practiced in primiparas. There were 5 mortalities, one a bad cardiac, one sudden death proved at autopsy to be pulmonary embolus, two deaths were due to sepsis, and one to a ruptured uterus, the result of the two-forceps maneuver in inexperienced hands.

Breech Extraction.—Breech extraction occurred 96 times with a fetal mortality of 20, an incidence of 20.8 per cent. There were no maternal deaths in this group. In the absence of any urgent indication for hastening the delivery we have not favored "breaking up the breech," but have permitted it to deliver as such.

Version and Extraction.—Version and extraction was performed 72 times, with a fetal mortality of 25 per cent and one maternal death in a case of placenta previa.

Cesarean Section.—There was a total of 129 cases, an incidence of 1.29 per cent, with 5 deaths, a mortality ratio of 3.92 per cent. Contracted pelvis were the indication in 60 per cent of all cases; 24 were done for cardiac decompensation, 17 for disproportion, 8 for placenta previa, 5 for eclampsia, and 6 for preeclamptic toxemia. The classic operation was performed on all elective cases, the low 2-flap operation on all patients in labor or with ruptured membranes. There was some type of morbidity present in 37 per cent of all classic sections as compared to 32 per cent in all the low cervical cases. However, it must be kept in mind that every patient in the latter group was given a trial test of labor. The morbidity rate increased in direct proportion to the time interval between the operation and the onset of labor plus ruptured membranes as shown so well in the survey of C. A. Gordon.²

Of the 5 deaths in this group, one could not be charged to the operative procedure. This occurred as a result of spontaneous rupture of the uterus in a para ix, ten hours in labor, who reached the operating table in a moribund condition. Of the remaining four deaths, two were due to pneumonia and two to sepsis. These latter two mortalities will be discussed under puerperal sepsis.

PUERPERAL SEPSIS

Among 36 deaths, there were 10 fatalities from puerperal sepsis, 7 in primiparas. This we attribute to the greater frequency of toxemia, protracted labors and need for operative interference in patients of this parity.

Prenatal Care.—Two of our 10 fatal cases of sepsis had well-marked toxemias of pregnancy on admission, while four others were observed to have had albuminuria ranging from 1+ to 3+. In two instances in which fatal sepsis occurred, no factor could be held responsible other than coitus within a day prior to rupture of the membranes. Examination of the male prepuce is mentioned by Irving³ as showing streptococci in about 75 per cent of the cases. Further, more emphasis should be laid on the necessity for reporting rupture of the membranes without the onset of pains. In two instances there was rupture of the membranes three days before the patient applied for admission and in one of these instances the patient had a temperature of 100.6° F. on admission. In this latter case, in spite of a rapid spontaneous delivery, the patient succumbed to puerperal sepsis. In the first case, because of obstructive dystocia, a low 2-flap cesarean section was performed. There is a question whether a Porro hysterectomy might not have saved this patient from a fatal sepsis.

The New York Academy of Medicine Committee on Maternal Mortality has shown puerperal sepsis to be five times as frequent following operative interference as compared with spontaneous delivery. In our ten deaths from sepsis, four patients had prolonged labors and five operative interferences with anesthesia. Adequate prenatal investigation should reduce the incidence of prolonged labors and diminish thereby the risk attendant to operative procedures.

Endogenous Infections.—Two of our women upon whom vaginal examinations had not been made during labor and who had been delivered spontaneously and quickly with the most approved aseptic technic, developed fatal puerperal sepsis. One of the patients was admitted with the caput slightly visible and protected by membranes. She developed a fatal peritonitis and hemolytic streptococci were cultured from the peritoneal fluid.

Causative Organisms.—In our 10 deaths, the blood culture was positive for hemolytic streptococci in three cases, for staphylococci in one case, for *B. coli* in one case, and for *B. welchii* in one case. Two cases had repeatedly negative blood cultures and in two cases blood cultures were not taken. In spite of the near proximity of the rectum to the internal genitalia, it is most unusual for puerperal sepsis to be caused by the gas bacillus.

Our fatal case of Welch Bacillus infection gave the following history: A forty-two-year-old para iii was admitted in premature labor with the membranes already ruptured. An amputation of the cervix had been done seven years previously. On physical examination the temperature, pulse, and respiration were normal. The cervix could not be felt on vaginal examination or seen on inspection with a speculum. Irregular pains were present on admission and continued for three days. On the third day there was a rise in temperature to 100°. Because of the presence of infection, operative interference was deemed contraindicated. On the following day the patient suffered a chill and a temperature of 102°. At this time the blood culture was positive for *B. welchii* and on this day she delivered spontaneously a premature stillborn fetus. The placenta could not be expressed. Eight hours postpartum a hysterectomy was performed for the purpose of removing the focus of infection feeding the organisms to the blood stream. Acriflavine and perfringens antitoxin were administered intravenously. She died on the sixth day postpartum. On histologic examination the extirpated uterus showed a septic metritis.

TOXEMIAS OF PREGNANCY

Preeclamptic Toxemia.—There was one maternal death, due apparently to the toxemia.

Eclampsia.—There were 58 eclamptics, of whom 34 were antepartum, 10 intrapartum and 14 postpartum. Among these, there were 4 antepartum and 1 intra-

partum deaths. All of the postpartum cases recovered. In this group 44 patients gave a negative history, 7 had a preexisting nephritis, 5 had toxemias in previous pregnancies. Thirty-five had had prenatal care, and 23 had no prenatal care. The treatment was expectant in all cases, with the exception of 4 patients who did not respond to medical therapy; these were terminated by abdominal delivery under local anesthesia. There were 26 stillbirths in this group. As noted above, 5 deaths occurred in 58 cases, or an incidence of 9 per cent. This compares favorably with the incidence of death in eclampsia by other authors and argues well for the conservative medical treatment which we have adopted as our routine in the treatment of this condition. In our experience, the intravenous administration of glucose, the intramuscular injection of morphine and magnesium sulphate have proved of unquestionable value.

The consideration of our five fatal cases as a group brings forth several points of interest.

1. *The High Incidence of Low Parity.*—Three of the deaths were in primiparas and two in para i, but this is merely a part of the high incidence of low parity for all cases. Thus 30 of our 58 cases were primiparas.

2. *The Prognosis Is Dependent Upon the Number of Convulsions and Their Time of Occurrence.*—In each instance in our series in which death occurred, the patient was admitted to the hospital after four or more convulsions had taken place. In 14 instances of postpartum eclampsia there were no deaths.

3. *The Importance of Prenatal Care in Prophylaxis.*—This is by far the most important point to emphasize. None of the 5 patients who died in this series received adequate prenatal care.

POSTPARTUM HEMORRHAGE

So far as maternal mortality is concerned, the third stage of labor is considered by many obstetricians to be the most dangerous, and mainly because of the frequency and seriousness of severe postpartum hemorrhage. It occurs about once in 100 cases, 95 times in our series of 10,000 cases. It is the most common cause of maternal death and it is generally conceded that more women die of postpartum hemorrhage than from placenta previa and premature separation of the placenta together. Yet in our series, we had but one death from this complication, although we have had four deaths from placenta previa and premature separation of the placenta.

RUPTURED UTERI

Two of the cases of ruptured uteri resulted fatally.

CASE 1.—This patient was a twenty-five-year-old primipara who had been in labor forty-three hours. There was a well-marked contraction ring. A two-forceps maneuver was attempted by an inexperienced operator. The patient went into shock and died forty-five minutes later. Death was due to rupture of the uterus. This fatality was preventable and was due obviously to the inexperience of the operator. It should serve to show that only adequate supervision of the work of the house staff by a capable attending staff can prevent a similar tragedy.

CASE 2.—The patient was a forty-four-year-old para ix, who had a vertex presentation; she had had ten hours of moderate labor pains and was 3 fingers dilated. For no apparent reason she suddenly became pulseless and went into extreme shock. The abdomen was rigid. No pituitary extract had been given. An immediate laparotomy revealed a rupture of the uterus at the cervicovaginal junction extending into the broad ligament. She died on the operating table. Microscopic examination of the uterus after removal showed leucocytic infiltration in the area of rupture.

In this last case, the complication occurred in a patient who was under observation in a hospital where all the facilities necessary for rapid treatment were available and yet death resulted. Transfusion and rapid laparotomy with hemostasis and repair, or hysterectomy, with little regard for the toilet of the operation, may save what appears to be a moribund patient.

PLACENTA PREVIA

Of 57 cases, 39 were of the marginal type, 11 partial, and 7 total. Of these, 8 were terminated by cesarean section. In the remainder, the bleeding was controlled by vaginal packing or Pomeroy bag followed by Braxton-Hicks version. Postpartum febrile morbidity occurred in 11 cases, of which 7 had vaginal packing prior to admission to the hospital. There were three maternal deaths. Two patients died of hemorrhage undelivered. In one of these patients transfusion might have saved the patient. She was a twenty-two-year-old primipara who was admitted because of irregular pains in the sixth month of gestation. There was no dilatation of the cervix and no bleeding at this time. Twelve hours after admission the patient suddenly suffered a severe hemorrhage. Vaginal examination showed the cervix to be 2 fingers dilated and a partial placenta previa. A second severe hemorrhage occurred and the patient died eighteen hours after admission.

This case illustrates the danger of a vaginal examination unless the examiner is prepared to treat the patient for placenta previa, as this procedure commonly precipitates a severe hemorrhage. In the face of one severe hemorrhage a compatible donor should have been secured and a transfusion given before attempting vaginal examination.

The third death occurred in a patient who died suddenly one hour postpartum, presumably of an embolus. This case also must be discussed more fully, for there is danger in the handling of such a patient that must not be disregarded. The case history will be found in the section on pulmonary embolism.

We have been favorably inclined toward the recent trend of abdominal delivery in all cases of the totalis type and selected cases of the partialis type.

PREMATURE SEPARATION OF THE PLACENTA

There were 18 cases, of which 4 were of the severe type, as manifested by extreme shock and anemia, 3 were moderately severe and 11 were of the mild type. Nine patients were treated expectantly, three had a bag induction and delivered spontaneously, one was terminated by forceps, one by breech extraction, one by version and breech extraction, and two by abdominal route.

There were two maternal deaths, an incidence of 11.1 per cent. One woman died undelivered. She was admitted to the hospital in a grave condition, following one week of pain accompanied by constant oozing. Autopsy revealed partial separation of the placenta. The second fatal case was that of a para ii who was admitted in shock and showed no external bleeding. The uterus was spastic and tender. The membranes were ruptured artificially, and there was moderate bleeding as a result. After four hours of labor she spontaneously delivered an eight-month fetus. Following spontaneous delivery of the placenta, the patient had a profuse uncontrollable hemorrhage and died. In retrospect, this case could have been better controlled by immediate abdominal delivery.

PULMONARY EMBOLISM

There were three maternal deaths from this complication. The factors that may have been responsible for the three fatalities from this tragic accident differ widely. One death occurred in a twenty-two-year-old primipara who, after forty hours of

labor, was delivered by midforceps. Following a manual removal of the placenta the patient suddenly went into shock and died. The case reports of the remaining two deaths will be presented in some detail, and will emphasize, in part, the prophylaxis of pulmonary embolus.

CASE 1.—H. H., twenty-nine years old, para i, at term, was admitted in labor. The blood pressure was 120/90, and albuminuria was absent. There was a cysto-rectocele and bilateral laceration of the cervix. After six hours of labor she was delivered spontaneously of a normal infant. On the seventh day postpartum the uterus was found to be two fingers above the symphysis pubis, there was a slight serosanguineous lochia and the general condition of the patient was good. The puerperium up to this period had been afebrile. Under spinal anesthesia an anterior colporrhaphy, posterior colporrhaphy, and trachelorrhaphy were performed. The patient was returned to her bed in good condition. Eleven hours postoperative, the patient was restless and vomited. The temperature was 100.4°, the pulse 114, the respiration 22. It was felt that the patient was experiencing a customary postoperative reaction. Three and one-half hours later she was found dead in bed. The house doctor noted that this was the most sudden unexpected death he had ever witnessed.

CASE 2.—M. B., a twenty-year-old primipara, at term, was admitted with the history that she had been in labor for several hours. She had been attended by a midwife who became alarmed by a profuse hemorrhage and called an ambulance. When first seen on admission she complained of nausea, headache, and weakness. She was pale, dyspneic and slightly cyanotic. The pulse was rapid and thready and the extremities cold. The blood pressure was 95/50, and the hemoglobin 32 per cent. There were occasional uterine contractions. The fetal heart sounds were faint, the rate about 100. On rectal examination the cervix was felt to be soft and no dilatation could be made out. The presenting part could not be felt and a soft boggy mass was palpated. A diagnosis of placenta previa centralis was made and the patient observed for about eighteen hours. During this period, therapy included digifolin and morphine by hypodermic, but no transfusion or intravenous infusions.

A version was finally decided upon and under general anesthesia both feet were brought down. The patient was then allowed to come out of the anesthesia and deliver herself spontaneously in one-half hour. The hemoglobin was 25 per cent after delivery. Although the patient's general condition was considered poor, it was not alarming. On being moved from the delivery table on to a stretcher soon after delivery, the patient suddenly became more cyanotic, suffered a generalized seizure and died. The object lessons to be learned from this case are the following:

1. In the face of a history of a severe hemorrhage and a patient showing the signs of an acute anemia, a transfusion obviously should have been given soon after admission.

2. It is our impression that the actual cause of death was pulmonary embolus precipitated by moving the patient too soon after delivery in a case of placenta previa. With this condition there must be even greater engorgement in the pelvis than occurs with a normal implantation of the placenta. Since this particular tragic accident occurred we have been careful to adhere to the rule of allowing the patient to remain for at least one hour on the table following this type of delivery.

3. With a central placenta previa in a primipara, a cesarean section should be the treatment of choice.

CARDIAC DISEASE

We had 70 cases of cardiac disease, 6 of the patients were decompensated; 21 were delivered spontaneously, 4 by cesarean section, 1 by breech extraction and the largest

number, 42, by forceps. Two remained undelivered. There were 4 deaths due to this complication. Since such deaths occur in nongravida, this is not a high incidence for a series of 10,000 cases. Three patients were para ii and one was a primipara. Their ages ranged from twenty-one to forty-two years. One patient died before delivery, 2 within six hours after delivery, and 1 on the third day postpartum.

It is noteworthy that three patients died soon after admission to the hospital. This must mean inadequate prenatal care. A cardiac who becomes gravid must be observed carefully during the entire length of gestation for any indication of impending decompensation and then promptly hospitalized.

MISCELLANEOUS CAUSES OF DEATH

1. *Pneumonia*.—There were 4 deaths due to pneumonia, two of the lobar type and one of these was further complicated by diabetes. The remaining two deaths were of the bronchopneumonia type and occurred after cesarean section.

2. *Tuberculosis*.—There were five cases of pulmonary tuberculosis in the entire series. Three patients were delivered spontaneously and two by low forceps. One of the patients delivered spontaneously died of miliary tuberculosis.

3. *Diabetes*.—There were nine cases of diabetes in the entire series. One patient was delivered spontaneously and eight by operative procedures. In one death diabetes complicated a lobar pneumonia. This case has been mentioned above.

4. *Spinal Anesthesia*.—There was one death wholly from this cause. It occurred in a patient who was being anesthetized for a cesarean section. Since the recent trend of accepted opinion that the risk attendant to spinal anesthesia is of major proportions, we have discontinued its use, except in definitely selected cases.

The compilation of these data was completed with the assistance of Dr. Elmer Gergely and Dr. Aaron J. Orloff and credit is gratefully acknowledged. I am likewise indebted to Dr. Leo Schwartz, Chief of Service, for the privilege of reporting this material and for his generous cooperation in the final preparation of this paper.

REFERENCES

- (1) Maternal Mortality in New York City, 1930-1932, Commonwealth Fund Publication, New York, 1933.
- (2) Gordon, C. A.: AM. J. OBST. & GYN. 16: 307, 1928.
- (3) Irving, F. C.: Outline of Abnormal Obstetrics, Ann Arbor, Mich., Edward Brothers, Inc., p. 141.

875 ST. MARKS AVENUE

Clark, H. C.: Prenatal Care, Am. J. Surg. 25: 390, 1934.

In spite of improved prenatal care, reliable statistics prove that the maternal mortality rate has not been decreased, because the good work of the trained and skilled physician is overbalanced by the poor work of the unskilled and unscientific practitioner. It is the duty of every physician to help improve the maternal mortality rate by educating the laity to demand better obstetrics.

J. THORNWELL WITHERSPOON.

THE DETERMINATION OF URINARY HISTIDINE AS A CHEMICAL TEST FOR PREGNANCY

THEODORE R. SEIDMAN, M.D., ROCHESTER, N. Y.

(From the Department of Obstetrics and Gynecology, the University of Rochester,
School of Medicine and Dentistry)

IN 1929 Voge¹ described a chemical test for pregnancy based on Knoop's test for histidine, performed simply by boiling urine with bromine water, which, in a small series of 60 cases, gave a 95 per cent correlation with the Aschheim-Zondek test.

The accuracy of this test would appear to have been amply disproved by the work of later investigators^{2, 3, 4} who, with much larger series, found only 63 to 75 per cent positives in pregnancy, with from 8 to 16 per cent of false positives among the controls.

However, Knoop's test for histidine, as applied to urine, is far from satisfactory. The color change is usually by no means striking, and its intensity depends upon the general composition of the urine, rather than upon its histidine content alone. Some urines give an intense reaction with histidine concentrations of less than 1:20,000, whereas others may show a scarcely detectable change with histidine concentrations over 1:5,000.

In view of the fact that histidine, in small amounts, is a normal constituent of urine, it was felt that such a qualitative test could never determine the ultimate value of histidine excretion as the basis for a pregnancy test. Therefore it seemed worth while to run a series of cases, using a procedure which should be at least roughly quantitative.

During the pursuit of this investigation interesting questions arose as to the possible significance of this phenomenon. These cannot be answered in the present paper, which deals only with the practical aspect of the problem.

Experimental.—The method of determining histidine employed in this series is a simplification of that described by Kappel-Adler.⁵ Reagents necessary are:

- (1) Hopkins' reagent (a solution of 10 per cent mercuric sulphate in 5 per cent H_2SO_4).
- (2) A solution of 2 parts concentrated NH_4OH and 1 part 10 per cent $(\text{NH}_4)_2\text{CO}_3$.
- (3) A solution of 1 per cent bromine in 33 per cent acetic acid.

Ten cubic centimeters of urine are transferred into a 15 c.c. centrifuge tube, and the remainder of the tube filled with Hopkins' reagent. The precipitate is spun down and the supernatant fluid poured off. Enough distilled water is added to bring the total volume up to 2 or 3 c.c. The precipitate is then decomposed with H_2S , agitating with a stirring rod until a uniform inky black suspension is obtained. The

precipitated mercuric sulphide is spun down and the clear, colorless or yellow fluid is poured off into a clean graduated tube. The H_2S is expelled by bubbling air vigorously through the solution for about thirty seconds. The bromine is then added drop by drop until the solution remains bright yellow. Frequently the solution first becomes pinkish and then yellow upon further addition of bromine. After ten minutes 2 c.c. of the ammonia mixture are added and the solution heated for one minute on the boiling water-bath. The solution is cooled, made up to 10 c.c. volume, and the color, ranging from a light pink to a deep purple, is compared in the colorimeter with the color developed by 1 c.c. of a standard solution containing 1 mg. of histidine. The comparison should be made without delay, as in some urines the color fades rapidly.

The precipitation of histidine by Hopkins' reagent appears to be partially a "dragging down" effect. Histidine cannot be satisfactorily recovered in this fashion from pure water solution or from urine which is too dilute to yield 0.5 c.c. of precipitate (below sp. gr. 1.012). Too concentrated urines should be diluted before analysis because of the intensity of the interfering brownish color which otherwise develops. The presence of large amounts of albumin or salicylates render the determination unsatisfactory by preventing the bromination of histidine.

No claims are made for this procedure as an accurate analytical method. Colors developed in urine seldom compare exactly with the standard because of the admixture of a yellowish tinge. Recoveries from concentrations above 1:20,000 vary from 80 per cent to 100 per cent. However, any more exact method would be much more laborious, and under the conditions of the experiment, could add little to the significance of the results.

Samples were taken from specimens collected routinely on the wards or in the outpatient departments of the hospital. Specimens obviously too dilute were either discarded or subjected to preliminary concentration on the steam bath. The least readily detectable amount of histidine was considered to be 5 mg. per cent since colorimetric readings below this figure are not significant.

Determinations were made upon specimens from 199 female subjects: 102 pregnant and 97 nonpregnant. In the pregnant group 94 were positive and 8 were negative. In the nonpregnant group, 24 were positive and 73 negative. Thus the test was positive in 92 per cent of pregnancies but yielded 25 per cent of false positives. That the accuracy of the test cannot be improved by setting up any arbitrary level of histidine concentration as significant, is shown in Table I.

TABLE I

Minimum conc. of histidine	50 mg. %	40 mg. %	30 mg. %	20 mg. %	10 mg. %	5 mg. %
Pregnant	6	10	15	34	73	94
Nonpregnant	0	0	1	3	10	24

The quantities of histidine excreted bore no evident relationship to the duration of the pregnancy. Two negatives were obtained during the first trimester, three during the second, and the other three at term. The earliest positive result obtained was at six or eight weeks. The unusually high levels of histidine excretion were found scattered throughout the period of gestation. Only two patients were followed after parturition. They were still positive at two weeks and were negative at three weeks.

The controls used in this series were not normal, but included the general run of the wards and clinics, selected only in regard to child-bearing age. Positive results were obtained in 4 out of 6 cases of pelvic infection, 2 out of 4 myomas, and 3 out of 9 postoperative cases. However, positive results were also obtained in 7 out of

15 cases whose complaints had to be classified as "functional." The other positive results represented as many different types of disease. Ovulation tests were carried out whenever there appeared to be the slightest possibility of pregnancy.

As a matter of curiosity, determinations were made upon a few male specimens, with the interesting result that considerable quantities of histidine were found in 3 out of 4 cases of undescended testicles. Ovulation tests performed with 2 of these specimens were negative.

DISCUSSION

It is obvious from the above experiments that the quantity of histidine in a single urine specimen cannot serve as the basis for a satisfactory pregnancy test. Whether or not more striking differences might be demonstrated by histidine balance studies over extended periods, is of theoretical interest only, since the test would then become too cumbersome to replace the highly successful rabbit ovulation test.

Little is known of the metabolism of histidine, and no explanation can be offered for its increased excretion in the urine. That this is in some way influenced by the sex hormones is apparent from its high association with pregnancy in the female, and with undescended testicles in the male. It is equally apparent from the negative ovulation tests obtained with urines of high histidine content, that histidine is not necessarily excreted in any intimate relation to the hormones of pregnancy.

CONCLUSION

The excretion of histidine in the urine merits further study as an interesting biochemic phenomenon, peculiarly characteristic of the pregnant state. However, it is not specific enough to serve as the basis for a reliable pregnancy test.

The author wishes to express his thanks to Dr. C. A. Elden for aid and encouragement in this work.

REFERENCES

- (1) *Voge, C. I. B.*: Brit. M. J. 1: 829, 1929. (2) *Young, A. M.*: J. Lab. & Clin. Med. 19: 153, 1933. (3) *Dodds, G. H.*: Brit. M. J. 1: 948, 1930. (4) *Siddall, A. C., Hui, S. F., Ha, H. W., and Wong, W. H.*: China Med. J. 45: 646, 1931. (5) *Kappel-Adler, R.*: Biochem. Ztschr. 264: 131, 1933.

Holzappel, K.: The Treatment of Climacteric Bleeding With Vaporization, Monatschr. f. Geburtsh. u. Gynäk. 97: 269, 1934.

In the treatment of climacteric hemorrhage there are five measures which may be used, namely, medical and endocrine therapy, curettement, vaporization, irradiation and extirpation of the uterus. In most cases, especially the mild ones, medical and endocrine therapy are employed. If no relief is obtained, the suspicion of carcinoma is aroused and a curettement is performed. In most instances, however, this operation is not curative and thus the choice lies between vaporization, irradiation and removal of the uterus. The last is the most radical whereas vaporization is the simplest. Holzappel has employed vaporization 111 times in the last thirty-two years, and among these cases he encountered two fatalities. He describes the technic he employs.

J. P. GREENHILL.

ANALYSIS OF ONE HUNDRED AND FORTY-SIX CASES OF PLACENTA PREVIA*

JAMES P. MARR, M.D., F.A.C.S., NEW YORK, N. Y.

(From the Clinic of New York Nursery and Child's Hospital)

LAWSON TAIT in 1899 advocated cesarean section for placenta previa. This radical departure aroused a violent storm of criticism and opposition from a conservative profession. Even today, there is great reluctance to accept this procedure in such celebrated centers of midwifery as the Rotunda, in Dublin, and Queen Charlotte's, in London. But a more surgically minded generation has accepted Tait's innovation which has gradually won itself a place in the treatment of an obstetric complication where both mother and child are in serious jeopardy. In 1931, Bill of the Cleveland Maternity Hospital published his series of 104 placenta previas, 79 per cent treated by cesarean section showing the lowest maternal and fetal mortality of any large series. This led me to review the cases of placenta previa treated at the New York Nursery and Child's Hospital, in hope that some light might be thrown on the relative values of the different methods of treatment, especially as the work of many operators would subject any one maneuver to a critical test.

The following report is based on a study of one hundred and forty-six patients with placenta previa which occurred during the past fifteen years, from 1918 to 1932 inclusive. The incidence of frequency of this complication was one in 278 patients which corresponds closely with other published reports of hospital series. On the basis of the recognized divisions of placenta previa, there occurred in this series, 32 central, 39 lateral, and 75 marginal placenta previas.

METHOD OF DELIVERY IN CENTRAL PLACENTA PREVIA

Of the 32 patients presenting central placenta previa, 19 (15 per cent were subjected to cesarean section with no maternal mortality and 21 per cent fetal mortality. Of these 6 had occurred in primiparas and 13 in multiparas. Five patients (15 per cent) were subjected to bagging, followed by internal podic version, with no maternal mortality and 40 per cent fetal mortality. Two patients were subjected to an internal podalic version with one maternal death (50 per cent) and 100 per cent fetal mortality. Two patients were subjected to bagging, accouchement forcé and followed by a breech extraction, with one maternal death (50 per cent) and 100 per cent fetal mortality. One patient was subjected to bagging, and followed by a

*Read before the Medical Society of the County of New York, April 27, 1934.

breech extraction with one fetal death. One patient was subjected to bagging, accouchement forcé followed by a version, the patient and child survived. Two patients were subjected to accouchement forcé and version, with no maternal mortality and one (50 per cent) fetal mortality.

METHOD OF DELIVERY IN LATERAL PLACENTA PREVIA

There were 39 patients presenting lateral placenta previa with no maternal deaths. Of these, three were treated by cesarean section, two were primiparas and one was a multipara. Six patients were subjected to bagging, followed by an internal podalic version, with a fetal mortality of 83 per cent. Six patients were subjected to bagging, followed by forceps, with a fetal mortality of 16 per cent. In 16 patients the membranes were ruptured artificially, followed by a normal delivery or forceps, with 3 fetal deaths. Four patients were subjected to an internal podalic version, with 4 fetal deaths. Two patients were subjected to accouchement forcé and forceps, with one (50 per cent) fetal death. Two patients were subjected to bagging and followed by normal delivery, both babies died.

METHOD OF DELIVERY IN MARGINAL PLACENTA PREVIA

There were 75 patients, presenting marginal placenta previas with 5 maternal deaths. Of these, 18 patients (24 per cent) were subjected to cesarean section, one mother died on the eighth postoperative day, following a transfusion, giving a maternal mortality of 5 per cent and fetal mortality of 20 per cent. Thirteen of these were primiparas and 5 multiparas. Twenty-one patients were subjected to bagging, followed by internal podalic version with one maternal death (4.7 per cent) and 52 per cent fetal mortality. Fifteen patients were subjected to simple rupturing of the membranes or combined with forceps, with no maternal mortality but 50 per cent fetal mortality. Five patients were subjected to bagging, followed by forceps with one maternal death and one fetal death. Five patients were subjected to accouchement forcé and forceps, or internal podalic version with 2 maternal deaths and 3 fetal deaths. Four patients were subjected to an internal podalic version, with no maternal deaths and one fetal death. One patient received a Braxton Hicks version; the mother lived, the fetus died.

There were a total of 40 cesarean sections in this series which included thirty-two classical operations, three low flaps, two peritoneal exclusions, one Porro and two vaginal hysterotomies. The vaginal hysterotomies were performed on primiparas, one at term, one at the twenty-seventh week, both were of the marginal type.

There was one maternal death in this group of 40 cesarean sections, but it cannot be attributed to the operation, rather to the incompatible blood administered on the eighth postoperative day. Assuming that cesarean section is a radical procedure, it carried the least maternal mortality and the least fetal mortality. On the other hand the conservative method was employed on 32 occasions in which the membranes were ruptured artificially, followed by a spontaneous delivery or by forceps. There was no maternal mortality but the fetal mortality was 37.5 per cent.

Between these two groups, the one treated by cesarean section, the other, conservatively, there was an intermediate group, consisting of 73 patients, which were treated rather vigorously. Twelve patients received accouchement forcé with 3 maternal deaths (25 per cent) and 6 fetal deaths. In 50 instances the bag was the initial procedure followed by version or forceps, with two maternal deaths (4 per cent) and 25 fetal deaths. Ten patients were subjected to internal podalic version, with one maternal death (1 per cent) and a fetal mortality of 70 per cent. One Braxton Hicks version was performed, the mother survived, the fetus was stillborn.

ANALYSIS OF MATERNAL DEATHS

A brief review of the fatalities reveals that five patients died before leaving the operating room of a combination of hemorrhage and shock. One patient died immediately on receiving incompatible blood on the eighth day and one patient died of sepsis on the thirty-first day. All these patients entered the hospital in good general condition; by that is meant, they were not exsanguinated or infected from previous vaginal manipulations.

A. R., para i, aged twenty-two, at term, vertex, marginal previa, low classical cesarean section, received a transfusion immediately following delivery. On the eighth day, a second transfusion proved fatal due to incompatibility.

M. G., para vi, aged thirty-five, eight months, vertex, central previa, was three fingers dilated, soft, thin, bleeding briskly, received accouchement forcé and internal podalic version. Ran a definite septic course and died on the thirty-first day postpartum.

M. Q., para i, aged thirty-five, at term, vertex, marginal previa, three-finger dilatation, a No. 4 bag inserted, followed by forceps after a long hard labor. Bled profusely following delivery, was packed and repacked, transfused but died in operating room of hemorrhagic shock.

D. G., para i, aged thirty-three, seven and one-half months, breech, central previa, two-finger dilatation, a No. 4 bag inserted followed by a breech extraction, bleeding profusely, packed, infused but died in operating room of hemorrhagic shock.

D., para i, aged thirty-six, nine months, vertex, three-finger dilatation, marginal or low implantation. Slowing fetal heart, the cervix was incised anteriorly and followed by forceps. The patient died just as transfusion was started; cause, hemorrhagic shock.

H., para ii, aged thirty-one, eight and one-half months, vertex, marginal previa, two-finger dilatation, a No. 4 bag and followed by internal podalic version, bleeding profusely, packed, transfused and infused. Died shortly of hemorrhagic shock.

W., para iv, aged thirty-six, nine months, vertex, almost fully dilated, received internal podalic version with laceration of cervix extending into broad ligament and died in operating room of hemorrhagic shock.

SUMMARY

In this series of 146 patients with placenta previa in 33,464 deliveries, or an incidence of one in 278 patients, there were 56 primiparas and 90 multiparas. Bleeding occurred at term in 71 patients. Uterine and vaginal packing postpartum was deemed necessary in 60 patients (41 per cent). Of the 40 cesarean sections, 16 received uterine packing following removal of the placenta. Transfusion was performed on 31 occasions, twelve patients were transfused antepartum.

There were 7 maternal deaths (4.7 per cent). Five patients died of hemorrhagic shock. One patient died of sepsis and one patient died following a transfusion of incompatible blood. The uncorrected fetal mortality was 53 per cent.

A significant fact is that the maternal mortality from central placenta previa and marginal placenta previa is 6.2 per cent and 6.6 per cent respectively.

The maternal mortality in cesarean section is 2.5 per cent in contrast to 5.6 per cent in delivery by vaginal route.

The fetal mortality is 20 per cent by cesarean operation and 49 per cent by the vaginal methods.

CONCLUSIONS

Rapid dilatation of the cervix with immediate extraction of the fetus, i.e., accouchement forcé, is an unwise and unsatisfactory procedure. No matter what the disguise, it is a maneuver which should be unreservedly condemned.

The intrauterine bag produces results similar to those following accouchement forcé, these bad results are due to the blood loss before bagging, the trauma at insertion, and last, and of greatest importance, the considerable postpartum hemorrhage.

There are selected cases of marginal placenta previa, with adequate dilatation of the os, and engagement of the head, where artificial rupture of the membranes, with forceps delivery, is safe for the mother but entails a high fetal mortality. Under the same conditions, internal podalic version can be employed for an unengaged head with the knowledge that the fetal mortality is very high, 70 per cent in this series.

Injury to the involved lower uterine segment is avoided by cesarean section, and this is the crucial point. Trauma, shock, uterine atony, and the inevitable postpartum hemorrhage are thereby circumvented. Timely blood transfusions and the more extensive use of cesarean section will lead to a notable reduction in the maternal and fetal mortality.

It is submitted that given a patient with placenta previa and a viable child, abdominal cesarean section gives the best results and calls for the least display of obstetric virtuosity.

40 EAST SIXTY-FIRST STREET

OVARIAN PREGNANCY

WILLIAM C. THRO, M.D., NEW YORK, N. Y.

(From the Cornell University Medical College)

IN NONE of the cases of ovarian pregnancy reported has the gestation sac been completely surrounded by a corpus luteum, although lutein cells have often been found in the wall of an ovarian hematoma and might be considered as strong circumstantial evidence that the pregnancy had developed in a graafian follicle. In this instance the chorionic villi, as in practically every case reported were found lying free in a blood clot. The whole paraffin imbedding block was sectioned in an attempt to locate the embryo but the search was unsuccessful. It is generally concluded that the pregnancy is of short duration and the early death of the embryo is due to hemorrhage with a rapid degeneration of the embryo. The embryo may be

lost in the early rupture of the gestation sac. According to Hunter⁴ an embryo was not found in 24 of the 43 cases reviewed by him.

Mrs. M. Y., No. 532, housewife, aged thirty-six years. Chief complaints were vaginal bleeding and pain in the lower left quadrant of the abdomen. Her past history was negative and there was no history of tuberculosis, cancer, or hemophilia.

The patient began menstruating at thirteen, duration of periods six days. She has had four children, all living and well; all the deliveries were normal, forceps not being used on any. She has never had any miscarriages.

For the last two months, preceding the operation, the patient complained of sharp pains in the lower left quadrant, these pains coming on only when the patient sat down or when she went to stool. Vaginal examination revealed a soft mass in the left side.

At operation, a left salpingo-oophorectomy was performed. At the operation, blood clots were found in the left side of the abdomen and in the culdesac. The



Fig. 1.—*c.l.*, corpus luteum; *c.v.*, chorionic villi.

left tube was enlarged and there was a blood clot at the fimbriated end. The left tube, together with the left ovary, were removed. The right tube and ovary were examined and found absolutely normal.

Pathologic Findings.—Adjacent to the fallopian tube, there was a mass 3 by 5 cm. in size. Cross-section of this mass showed a thin capsule enclosing a bluish purple mass like clotted blood and through which there were small grayish areas. The greater portion of the piece of tissue sectioned consisted of a large hemorrhage surrounded by a wavy layer of corpus luteum cells. Most of the chorionic villi seemed to be outside of the ring of corpus luteum cells but in one section there were chorionic villi near the hemorrhage and inside of the narrow ring of corpus luteum cells. For the most part, the chorionic villi were in patches and surrounded by red blood cells. In one section, there was a small graafian follicle. In all the sections the superficial syncytial layer, the subjacent epithelial layer of Langhans, and the vascular mucoid connective tissue center of the chorionic villi were demonstrable.

I wish to thank Dr. Herman Lorber of St. Mark's Hospital, New York, for permission to publish this case.

Society Transactions

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF JUNE 22, 1934

The following paper was presented:

Maternal, Fetal, and Neonatal Morbidity and Mortality. Dr. Fred L. Adair.
(For original article see page 384.)

Dippel, A. L.: Death of Fetus in Utero, Bull. Johns Hopkins Hosp. 54: 24, 1934.

The incidence of fetal death in utero during the last trimester of pregnancy in series of 25,000 consecutive deliveries was 1.2 per cent. The incidence is higher in the colored than in the white race with a ratio of 2.6 to 1. With multiparity the incidence increases. The majority of intrauterine deaths occur some weeks before the estimated date of confinement. Patients with acute toxemia of pregnancy usually fall into labor soon after death of the fetus, while the duration of retention in other cases is usually longer. More male than female fetuses die in utero.

Signs and symptoms of fetal death usually are clear-cut, and consist of failure of the mother to feel movements, absence of fetal heart sounds and of normal fetal body tone, boggy fetal head, crepitation of skull bones, and retrogressive changes in the size of the uterus. Further suggestive symptoms often occur and include maternal nausea, malaise, headaches, foul breath, bad taste in the mouth, a pronounced uterine souffle, a fall in basal metabolic rate, and retrogressive changes in the breasts. Helpful adjuncts to diagnosis, but not altogether reliable, are found in the Aschheim-Zondek test and in roentgenograms. Acetonuria is not a constant finding.

The causes of intrauterine death in order of their frequency are: syphilis; toxemia; loops of cord about some fetal part; intercurrent maternal disease; acts of violence to the abdomen; induction of labor; hemorrhage; fetal anomalies; true knots in and torsion of the umbilical cord; unusual shortness of cord; localized constriction of the cord; incarceration of the uterus; and uterine anomalies.

The gross maternal mortality in the series was $\frac{1}{8}$ of 1 per cent and the corrected mortality $\frac{1}{16}$ of 1 per cent. The morbidity rate was 23.25 per cent as contrasted with 17.75 per cent for the general clinic population. It is seldom necessary to induce labor.

The character of the labor pains was not significantly different from those of the patient with a living fetus.

C. O. MALAND.

American Journal of Obstetrics and Gynecology

EDITORS: GEORGE W. KOSMAK, M.D., AND HUGO EHRENFEST, M.D.

Editorial Comment

Birth Control and Limitation of Population

THE term "Birth Control" undeniably is a misnomer, but by common usage has been accepted as meaning the limitation and control of conceptions and not of births. The thought of limiting population is rationalized, in the main, by two ideas. According to the one, limitation of offspring benefits the community, the state, or the race; according to the other, it accrues to the benefit of an individual—the mother—or of a family. The claim has been made that mass limitation of births was necessary because human reproduction advanced by geometrical, but the means of livelihood only by arithmetical, progression. This fact would result ultimately in actual overpopulation in relation to the means of sustenance.

It long was believed that excess population was retarded and prevented, and the desirable equilibrium maintained by the large loss of life through war, pestilence, and famine. With the deliberate reduction of these potent forces of destruction, population inevitably would be increasing. As a matter of fact, war as a means of direct destruction of human lives has persisted in its previous significance. Famine, largely the result of war and closely correlated distress, at least in certain parts of the world, continues as a destructive agent, especially of children. Pestilence alone has almost been eliminated.

All these three factors together tend to reduce population, but with characteristic difference in their respective actions. War itself destroys the healthiest and strongest members of society; pestilence and famine, on the other hand, more likely will eliminate those least able to withstand hardship. The difference between selective destruction by war, and mere mass elimination, more typical for famine and epidemic disease, is of importance.

Widespread information and practice of contraception will lead to mass prevention of conception. However, even here we can recognize

an element of selective prevention. The intelligent, more responsible and economically favored groups of society have a better knowledge of the important details of contraceptive technic and are more desirous and able to apply it. At present a general effort is being made to encourage groups lower in the economic scale to make wider use of contraception. It should be clearly understood, however, that while these lower groups are struggling for existence, under present conditions often in vain, they by no means represent the less or least desirable strata of modern society.

Selective limitation, furthermore, demands proper consideration of the biologic basis underlying the entire problem of eugenic control. As yet, we know comparatively little concerning the effect of eugenic principles on human life. There is much evidence pointing to the conclusion that the offspring of certain types of defective individuals carry with them inheritable characteristics which perpetuate these defective qualities in the human race, and may be highly undesirable in their effect upon the individual and society.

One might say that there are two major aims in any program for the limitation or control of reproduction. One objective would be the selective limitation, with the thought of eliminating gradually the more unfit elements and stimulating the production of the more desirable individuals in our social organization.

Progressive epochs in the development of the human race have been surrounded with varying conditions of life. These have modified the type of individual who is best fitted to survive in the environment of that particular epoch. Physical development and adaptability were more important to survival in primitive life than any intellectual or moral attributes. The weak perished and the strong survived under such conditions. There were deliberate attempts among some nations and peoples to destroy the weaklings who were regarded as a burden upon communal or family life. Gradually, the intelligence of individuals became more and more important, which induced man to depend on various devices discovered and created through the exercise of his intellectual powers. These discoveries and inventions gave man definite superiority over other forms of animal life and also gave certain races and nations superiority over others. They also provided for the survival of many who would have perished under less favorable influences.

Religious and humanitarian influences then came into play and led to a much higher valuation of human life. The assembling of large numbers of people in cities favored the development of pestilence and disease. These were rampant during the Middle Ages and resulted in marked reduction of population, but were gradually overcome, as already has been pointed out, by medical measures and improvements in sanitation.

Malthus enunciated his doctrine relative to the principles of population over one hundred and twenty-five years ago. He advocated discouragement of early and improvident marriages and the cultivation of self-restraint. Statistics would seem to indicate that certain sections of the world are overpopulated at the present day. As a matter of fact, effective reduction of mortality from various causes has produced a corresponding increase in the percentage of survivals, or, in other words, resulted in an increase of longevity. Concomitant with this reduction in mortality for the last half century, there has been a steady decline in the birth rate (as well as in the actual number of births) among a gradually increasing number of the more highly civilized nations. The birth rate in many of these nations already has reached a point where one could expect a practical equilibrium in the population. Probably no one, however, is in a position to state the ideal relationship between birth and death rates, either for a nation or for the entire world.

The most significant rôle in the limitation of offspring today presumably is played by the use of contraceptive measures. These methods are by no means new, and in some form have been applied since earliest recorded times. The underlying principles are relatively simple. Primarily, they depend upon the prevention of fertilization by interference with the union of ovum and spermatozoid. This may be accomplished by mechanical means, such as an occlusive pessary or condom; by interruption or occlusion of the ducts conveying these cells, such as the fallopian tubes or the vas deferens; by chemicals which destroy the germ cells; by a physiologic method which depends on the time relationship between ovulation and insemination; and, finally, by permanent elimination of productive faculty through sterilization or castration.

The other method of prevention of offspring, i.e., actually of birth, consists in the willful termination of pregnancy. The latter, not generally used among modern civilized people, constitutes feticide or infanticide, and not so rarely results in matricide.

Thus, such methods easily fall into two general groups: (1) The prevention of life, assuming that life begins with fertilization, and (2) the destruction of life. Deliberate termination of pregnancy involves either the destruction of the fetus or embryo before it has reached a state of development consistent with extrauterine life, or destruction subsequent to the attainment of viability.

Our profession today is confronted with problems of a limited propagation which involve important medical, as well as sociologic, aspects. The basic principles of the various methods are essentially medical, so far as the determination of their respective value and proper application are concerned. The physician faces two problems—the welfare of the individual and the welfare of society, both affected by the

wider use of such protective procedures. The dominant ethical principles of the medical profession are the cure and prevention of disease, the mitigation of all suffering, and the saving and prolongation of life. Its ethical attitude, therefore, of necessity is definitely antagonistic to any procedure which involves the destruction of life at any point of its existence. Any procedure implying such destruction can be adopted by the physician only if the destruction of the potential life of the fetus, in his belief, will prolong or save the life of the mother. There is a tendency among some nations to regard destruction of the fetus as fully justified if this be the desire of one or both parents, or for sociologic reasons. It is difficult for physicians to accept such unrestricted ideas and, indeed, they are averse to many religious doctrines and legislative enactments dealing with the matter involved.

Only a plan of prevention based on interference with fertilization by some of the methods above mentioned will appeal to the great majority of civilized peoples. A method, to be acceptable, must be harmless, efficacious, not too unesthetic, and must be quickly, easily, and generally applicable, even among individuals of low intelligence. The success of any contraceptive measure depends upon the cooperation of individuals sufficiently intelligent to employ the method properly.

There are two essentially different aspects to the question of contraception: First, the method may be used voluntarily by the individuals concerned; second, the method may be enforced on individuals for the purpose of controlling or preventing reproduction, if for social, medical, or eugenic reasons it is undesirable to perpetuate a certain type or species. Enforced prevention of offspring might be justified or desirable (1) for a group with definite hereditary stigmas which, in all probability, would be transmitted to the offspring and make them undesirable elements in our social organizations; (2) for a group with questionable hereditary stigmas, but who, in themselves, are a menace to society and thus subject their offspring to environments which would tend to develop them into the same type of extremely unsocial elements. However, for this last group there admittedly would exist another and probably preferable method of protection, namely, prompt separation of such children from their parents both in their own interests and that of society.

It is a debatable question how far economic considerations *per se* should enter into the problem of limitation of offspring. There would seem to be available another means of solving this problem—the establishment of an economic system which would eliminate poverty sufficiently to permit the proper rearing of offspring of those citizens who do not constitute hereditary or socially undesirable elements in our civilization.

There is little evidence that first-, second-, and third-born children are superior to those later in the order of birth. The lives of many

illustrious leaders seem to point to the contrary. We should strive to encourage propagation among desirable human groups and discourage it among the undesirables. Probably no concrete plan can be developed at the present time for attaining these goals, but these objectives should be among our thoughts, and the necessary plans for their gradual attainment should be laid.

We must solve these questions along certain general lines. It might seem almost axiomatic that no procedures should be adopted or utilized which are harmful to individuals or to society. We must decide for each individual case whether contraceptive advice, instruction and devices are to be furnished upon eugenic, medical or sociologic indications, or whether such means should be dispensed for no other reason than the mere request of the individuals immediately concerned. It is generally conceded that temporary or permanent sterilization, therapeutic abortion and similar procedures should have clear-cut and definite indications for their employment.

In all of this agitation, it is necessary to distinguish between individual rights and collective obligations. On the one hand, the privilege of the individual to do and conduct himself as he desires is granted. He may eat, drink, smoke and behave harmfully to himself and even to others as long as he wishes until he is checked by regulation for the protection of others or even himself. On the other hand, there is no obligation on other individuals or groups to furnish information or supplies which might accord with personal desires or wishes, especially if they are not for the best interest of the individual or of society.

It is, therefore, essential for the physician that he determine what is best for certain individuals and for society, and then attempt to proceed in accord with definite eugenic, medical and sociologic indications to the best of our present knowledge, thus leading to human betterment. Our acts as medical men and as public servants must be consistent with the best individual and collective interest. Sociologists should proceed along the same lines and establish and announce reasons, if such exist, for giving contraceptive instruction to individuals.

A policy of selective limitation of births by voluntary and compulsory methods controlled by recognized public servants and agencies is not unreasonable. Granting the right to manage individual behavior, there is no public obligation to abet an individual in the free exercise of his acts. There is a clear distinction between an individual right to obtain, and a public obligation to supply, information and instruction. Last, but not least, any mercenary motive in considering and solving these problems certainly should be vigorously eliminated.

—F. L. A.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Ectopic Pregnancy

Kriwsky, L. A.: The Extrauterine Pregnancies in the Njecajew Hospital in Leningrad, *Monatschr. f. Geburtsh. u. Gynäk.* 93: 292, 1933.

During five years (1927 to 1932) 168 cases of ectopic pregnancy were operated upon which with the previous 835 (between 1910 and 1926) make a total of 1,003 cases. In 56.6 per cent of the present series there was an external capsular rupture, in 35 per cent an internal capsular rupture, and in 8 per cent this point could not be determined with certainty.

A diagnostic pelvic puncture was rarely performed. In the treatment it was customary to be conservative. Usually only the involved tube was removed. Many of these women subsequently had normal intrauterine pregnancies whereas only five women (3 per cent) had a repetition of a tubal pregnancy. There were 4 deaths in the series of 168 cases, a mortality of 2.4 per cent. Three patients died of peritonitis and the fourth died from the anesthetic.

J. P. GREENHILL.

Siegel, P. W.: Etiology of Ectopic Pregnancy, *Zentralbl. f. Gynäk.* 57: 686, 1933.

The author is so impressed with the etiologic relation of previous operations, especially uterine suspension, to tubal pregnancy, that he states, "In a doubtful diagnosis of tubal pregnancy, special attention should be paid to a previous operative correction of uterine position," and that in such cases, "the possibility of a tubal pregnancy is enhanced."

WILLIAM F. MENGERT.

Osiakina, A. J., and Schmatok, K. D.: The Decidual Reaction in the Tube in Intrauterine and Tubal Pregnancies, and Its Significance for the Etiology of the Latter, *Monatschr. f. Geburtsh. u. Gynäk.* 94: 329, 1933.

The studies of the authors revealed that there is ordinarily no decidual reaction in the tube in the presence of an intrauterine pregnancy. On the other hand, in cases of tubal pregnancy, a decidual reaction does occur frequently and its function appears to be a protective mechanism against the invasion of the chorionic villi at the site of implantation. The decidual reaction cannot be regarded as an etiologic factor in the causation of tubal pregnancies. In 21 per cent of the cases examined, the decidual reaction developed irrespective of the location of the implanted ovum. In 8 per cent of the last 21 cases, the authors considered the decidual reaction to be the cause of the tubal pregnancy. A decidual reaction can only occur in a tube

where there is not a highly differentiated mucosa and in cases where the tubal mucosa resembles that of the uterus in structure. A lack of differentiation in the tubal mucosa is most likely dependent upon unfavorable conditions of living such as strong physical work, hunger and infectious diseases during the prepuberty period.

J. P. GREENHILL.

Bernhard, Erich: The Increased Frequency of Tubal Pregnancy and Its Causes, *Ztschr f. Geburtsh. u. Gynäk.* 105: 46, 1933.

Statistics prove that there is an increase in the number of tubal pregnancies in Basel. Many etiologic factors contribute in this increase. Among these are an increased gonorrhea morbidity, greater frequency of abortions, wide use of contraceptives, especially of the intrauterine type and the Kafka cap, and numerous local inflammatory conditions following chronic appendicitis. Only slight significance is given to the much accused hypoplasia of the genitalia in the etiology of ectopic pregnancy.

GROVER LIESE.

Dawydow, G. L.: Curettement of the Uterus for the Purpose of Interrupting Pregnancy in the Presence of Undiagnosed Extrauterine Gestation, *Monatschr. f. Geburtsh. u. Gynäk.* 91: 447, 1932.

The early stages of an intact extrauterine pregnancy cannot be diagnosed. It is only when disturbances arise that the correct state of affairs may be recognized. When a curettement is performed early in pregnancy, great care must be exercised because an ectopic pregnancy may be present. Dawydow reports a case where the uterus was curetted in the presence of an extrauterine gestation. In this case, as in many reported in the literature, the patient suffered no harm. According to the author the external bleeding which occurs in cases of ectopic pregnancy is due either to the uterine endometrium or to the escape of blood from the gravid tube. A disturbed ectopic pregnancy may run the course of a tubal abortion or a tubal rupture, or a combination of these two, as occurred in this case.

J. P. GREENHILL.

Hatleberg, C. B.: Diagnosis and Treatment of Ectopic Pregnancy, *Wisconsin M. J.* 31: 530, 1932.

Ectopic pregnancy is difficult to recognize and yet it supplies the operating room with more emergencies than any other lower abdominal lesion except acute appendicitis. Irregular vaginal bleeding is probably the commonest diagnostic symptom, as 84 per cent of the cases show vaginal bleeding. Pain is the next most important symptom. In about 85 per cent of the cases a soft boggy mass is palpable on the affected side. The leucocyte count will average about 14,000. Colpotomy is very helpful in differential diagnosis and sometimes the ectopic pregnancy can be removed through the vaginal incision. Salpingitis is the condition most difficult to differentiate from ectopic pregnancy. Uterine abortion usually shows more profuse bleeding and a more definite history of amenorrhoea. The treatment is immediate operation, removing the affected tube and controlling hemorrhage. The author suggests that a considerable part of the first shock is due to rupture of an abdominal viscus, rather than to any large loss of blood. Ether acts as a stimulant in these cases if used for a short period and is the anaesthetic of choice. The average mortality is about 4 per cent.

J. THORNWELL WITHERSPOON.

Sserebroff, A. I.: Types of Operations for Tubal Pregnancy, Arch. f. Gynäk. 148: 364, 1932.

Sserebroff reviews the literature in regard to the incidence of tubal pregnancy following removal of the opposite tube for tubal pregnancy. He concludes that the incidence of the occurrence of a second tubal pregnancy in the remaining tube is 5 per cent. In the Leningrad clinic the incidence was 4 or 5 per cent. In addition, over 52 per cent of women were sterile following the occurrence of one tubal pregnancy and 14 per cent conceived but aborted. For these reasons the author is firmly convinced that both tubes should be removed whenever a patient is operated upon for tubal pregnancy.

RALPH A. REIS.

Saass, Carl: A Recurrence of Tubal Pregnancy in the Same Tube Following a Previous Ectopic Pregnancy With Partial Resection and Ligation, Zentralbl. f. Gynäk. 54: 2590, 1930.

Although ectopic pregnancy can occur in any part of a tube, the author could not find another case in the literature of recurrence of tubal pregnancy in one and the same tube. Five years before the present admission a thirty-five-year-old woman had had an ectopic pregnancy removed from the ampulla of the left tube by simple resection of the ampullic end of the tube. The stump was ligated. She returned, having had no pregnancies in the five-year interval (at the previous operation the right tube and ovary were normal) with symptoms exactly similar to those of her preceding ectopic. An ectopic pregnancy in the stump of the left tube was found and the tube was removed. Removal of the whole tube should be the operation of choice.

WILLIAM F. MENGERT.

Schroderus, M.: Four Cases of Unruptured Interstitial Tubal Pregnancy, Acta obst. et gynec. Scandinav. 14: 48, 1934.

According to statistics of the last few years the frequency of interstitial tubal pregnancy probably is less than 1 per cent among all tubal pregnancies. In interstitial as well as in other forms of tubal pregnancies it is possible and advisable to distinguish between tubal rupture and tubal abortion. One hundred and nine cases of interstitial tubal pregnancy have been reported since 1925. The author adds three cases of his own, and describes the clinical picture of interstitial abortion in the initial stage. He emphasizes that the syndrome is comparatively uniform and characteristic. The early diagnosis of interstitial tubal abortion does not seem to be difficult to make.

J. P. GREENHILL.

Hasselblatt, Robert: A Case of Primary Abdominal Pregnancy, Zentralbl. f. Gynäk. 56: 404, 1932.

A twenty-four-year-old woman who had had an abortion two and one-half years previously, and an intraligamentous cyst on the right removed by a right salpingo-oophorectomy one year previously, entered the clinic complaining of sudden abdominal pain and fainting. She was in collapse apparently from an intraabdominal hemorrhage. At laparotomy the uterus was found enlarged to the size of a four months' pregnancy, and the left tube and left ovary were seen completely free and normal. On the right side the old operative site was smooth and unaffected. A 28 cm. living fetus was removed but died after a few minutes. The placenta was attached to the right side of the uterus which was removed in order to assure hemostasis. Serial

sections of the right uterine cornu were made and no evidence of a right tube or of any connection between the ovum and the uterine cavity was found. The author believes that this case satisfies Veit's criteria for a primary abdominal pregnancy which are: (1) the fetus must be living, (2) must be in a living connection with its matrix, (3) the tubes and ovaries must be free and independent of the ovum. The author has collected 33 such cases from the literature.

WILLIAM F. MENGERT.

Apajalahti, A.: The Fate of Women Operated Upon for Tubal Pregnancies, Acta obst. et gynec. Scandinav. 12: 329, 1932.

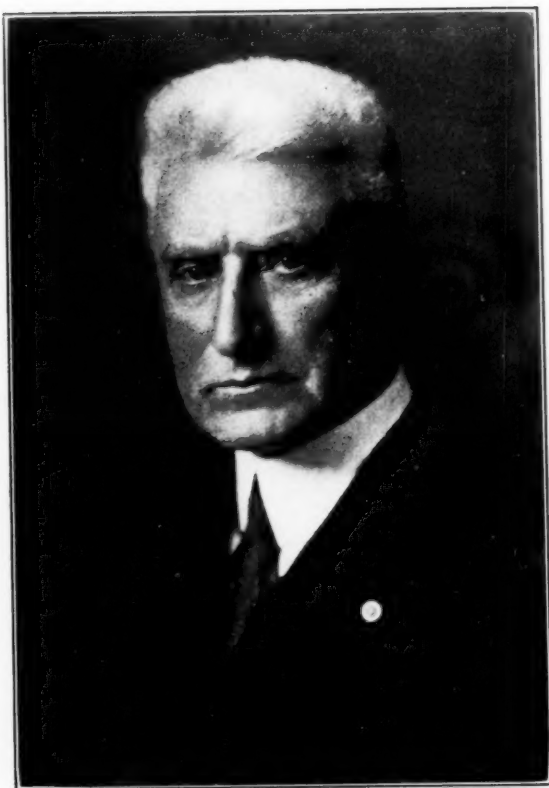
The author attempted to follow up a series of 300 women who were operated for tubal pregnancies from 1920 to 1930 at the Women's Clinic in Helsinki. Among 138 women who had hematoceles and adhesions at the time of operation he found that the type of operation played a distinct rôle in the subsequent health of the individual. Thus among those in whom the Beuttner high method of peritonealization was employed 88 per cent were free from annoying symptoms; whereas only 44 per cent of those in whom this type of peritonealization was not employed had no complaints. Furthermore, postoperative intestinal obstruction occurred in 3 out of 94 patients before the Beuttner method of peritonealization was employed, but no cases occurred among the 116 cases where it was used.

Among the 79 women who were capable of conceiving, 41 did become pregnant, and had 29 full-term deliveries, 20 abortions and 3 extrauterine gestations. The author adds that 18 women had two ectopic pregnancies. On the basis of a four years' interval, the frequency of repeated ectopic pregnancy was 7.3 per cent of the total number but if based only upon those who subsequently became pregnant the incidence was 17 per cent.

J. P. GREENHILL.

Dr. Franklin H. Martin

Dr. Franklin H. Martin died in Phoenix, Arizona, March 7. An extended obituary will appear in the April issue of the Journal.



(Moffett Studio)

FRANKLIN H. MARTIN
1857-1935